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THE SIGNIFICANCE OF CERTAIN INTERNAL CONDITIONS OF THE ORGANISM IN ORGANIC EVOLUTION

FIRST PAPER. THE REGULATION OF THE PHYSICO-CHEMICAL CONDITIONS OF THE ORGANISM[1]

F. H. PIKE AND E. L. SCOTT

DEPARTMENT OF PHYSIOLOGY, COLUMBIA UNIVERSITY

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THE desirability of an attack on the general problems of evolution from the point of view of physiology, as well as the general deficiency of literature in physiology bear-

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ing on these problems, has been recognized for some time.[2] The considerations to be presented in the papers of this series are in part the outgrowth of experimental work on the central nervous system and its relation to the processes of evolution;[3] they were in part suggested by Blackman's[4] paper on the manifestations of the principles of chemical mechanics in living matter; and they have gradually grown up in our minds as our attention was attracted more and more to the questions involved. The bearing upon the processes of evolution of certain of the facts drawn from the experimental study of the comparative physiology of the nervous system will, for the most part, be presented in separate papers embodying the experimental data. The relation of the physico-chemical conditions of the organism, together with those nervous mechanisms with which the maintenance of the physico-chemical conditions is inextricably bound up, to the questions of adaptation and fitness of the organism will constitute the greater part of the subject matter of this and following papers on the general problems of evolution from the point of view of the physiologist.

Since the inception of the work, there have appeared, in addition to Blackman's paper, several other papers of interest to physiologists on certain phases of the problem of evolution.

Woods[5] has collected the better-known cases of modification in animals and plants induced by changes in the environment or in the general conditions of existence, as shown by changes in the rate of growth, changes of the external form of the body, the occurrence of artificial

[2] Howell, "Problems of Physiology of the Present Time," Congress of Arts and Sciences, Universal Exposition, St. Louis, 1904, Vol. V, p. 11 of the reprint.

[3] Pike, *American Journal of Physiology*, 1909, XXIV, p. 124; *Ibid.*, 1912, XXX, p. 436; *Quarterly Journal of Experimental Physiology*, 1913, VII, p. 1; *Popular Science Monthly*, 1914, p. 403; *Science*, N. S., XI, p. 805.

[4] Blackman, *Nature*, 1908, LXXVIII, p. 556; AMERICAN NATURALIST, 1908, XLII, pp. 633–664.

[5] Woods, *Popular Science Monthly*, 1910, p. 313.

parthenogenesis, the modification of mental and moral traits, and the extent of regeneration of lost parts. When arranged in the order of their position in the taxonomic scale, organisms show a steadily decreasing response, with reference to these phenomena, to changes in the environment. Woods does not indicate, except in very general terms, the physiological mechanisms involved in bringing about this diminishing effect of the environment. Some years earlier Donaldson[6] had called attention to the general lack of influence of formal educational training upon the course of later life of talented individuals.

Julian Huxley[7] in his discussion of the individual in the animal kingdom, points out that the individual acquires an increasing independence of the environment, or that the environment has a diminishing effect. Huxley assigns mere increase in size and the increasing complexity and efficiency of the nervous system as two of the factors involved in the attainment of the freedom from mere accidents.

Mathews[8] has pointed out more specifically some of the various internal mechanisms which are involved in the acquisition of independence of the environment on the part of the higher animals. These are, according to him, (1) the heat-regulating mechanism, (2) the mechanism of immunity, (3) the mechanism for rendering animals independent of external conditions of moisture, (4) the mechanism which renders them independent of barometric pressure, (5) the mechanisms for reproduction and caring for the young, (6) the alimentary mechanism, and (7) the nervous system.

Henderson[9] has shown that the environment is an external thing in which certain physico-chemical conditions are kept relatively constant, while others may vary

[6] Donaldson, "Growth of the Brain," London and New York, 1895, pp. 347, 355, 360, 365.

[7] Huxley, J. S., "The Individual in the Animal Kingdom," Cambridge and New York, 1912.

[8] Mathews, AMERICAN NATURALIST, 1913, XLVII, pp. 90–104.

[9] Henderson, "Fitness of the Environment," New York, 1913.

widely, even in the same region. As long as organisms live in the ocean or in the water generally, they are subjected to certain relatively constant conditions dependent upon the physico-chemical properties of the environment. But it should be recognized that with organisms which have migrated out upon the land the case is somewhat different, as all conditions, except oxygen concentration and pressure, vary more markedly on the land than in the water. Temperature, in particular, varies greatly over the land, and the poikilothermal animals have their activities greatly limited by the temperature conditions.

From Henderson's premises, the conclusion follows that life is what it is because the environment is what it is. A different environment might, and in all probability would, have resulted in, or been associated with, a different form of life on the earth. Certain characteristics commonly called adaptations are, as Henderson shows, the automatic and inevitable results of the physico-chemical conditions obtaining in the environment. If such a view assumes that an adaptation ceases to be an adaptation when the manner of its origin is discovered, it would seem that we were in need of a more precise definition of adaptation. The question arises whether other similar characteristics that have been called adaptations are not also the inevitable and automatic result of the physico-chemical conditions of the environment. We may therefore consider the question of the reality of adaptation, and also whether some of the characteristics of organisms are not really adaptations,[10] even if they arise from the action of physico-chemical conditions in the environment. Again, since, in a given environment, with essentially the same physico-chemical conditions for all its inhabitants, there are many animal types, it would appear that there were some influences operative within the organism itself to produce certain characteristic reactions, known as adaptations, to the environment. As we will show subsequently, these facts do not in any way preclude an explanation of their origin on some hypothesis

[10] Mathews, *loc. cit.*

other than vitalism. The organisms may be, under certain conditions at least, more variable than the environment. These considerations apply also to those simple organisms which are the cellular constituents of a larger body. Certain of the higher vertebrates, in which, as has been indicated, the influence of the environment is probably less than in some of the lower forms, are more variable than certain of the lower vertebrates.

It is a fair inference from the facts cited in the various papers referred to, that certain characteristics of living matter, such as its slight degree of alkalinity, and its relatively great specific heat, may be regarded as the direct automatic and inevitable results of the properties of the environment. Other characteristics, as the peculiar type of the nervous system, are not so obviously the direct and inevitable result of the environment, and these may be regarded, for some time to come, as adaptations to the environment or to the general conditions of existence in which the particular organism is able to live and perpetuate itself.

A statement of the general problem may now be made. Two general classes of organisms live in a relatively constant environment, so far as the general internal conditions of the organism are concerned. (1) For example, the lower marine organisms of fairly limited distribution live in an external environment which changes but little in temperature, osmotic pressure, inorganic salt content, neutrality or faint alkalinity, oxygen and carbon dioxide concentration, and soluble nitrogen compounds. Temperature and amounts of light may vary somewhat throughout the year, but the temperature changes in the given region of the ocean are less in magnitude than the temperature changes over a corresponding area of land. The osmotic and inorganic salt relationships of organism and environment alike vary but little. Nor does the organism, in general, maintain within itself, any purely physico-chemical condition differing greatly from that in the general external environment. This does not pre-

clude the origin within the marine organism of stereochemical isomers, the great importance of which has recently been pointed out by Reichert.[11] Stability of conditions would even favor the perpetuation of such compounds as could be formed under a given set of conditions. (2) On the land, as has already been indicated, the higher animals—birds and mammals—have acquired a relative independence of the environment as shown by their wide distribution. Their internal conditions of temperature, moisture and the like, may not only differ greatly from the same conditions in the environment at any given time, but the internal conditions, as we shall show, do not change greatly when the external conditions change. Intermediate between these two types is a third type which lives in an environment subject to wide variations of temperature and moisture, and whose internal temperature varies with the change of external temperature. While some of the internal conditions of these organisms remain relatively stable, others are subject to wide variation. We have then to explain, in terms of function, (1) what are the various mechanisms by which the higher animals have attained this relative independence of the environment and (2) what has been the rôle of these mechanisms in organic evolution.

II. The General Constancy of Internal Conditions in the Higher Organisms

The study of the internal physico-chemical relationships of higher animals has led to the acquisition of a considerable mass of facts concerning this phase of animal organization. These facts show that in the higher animals there exist a number of mechanisms which interact to bring about a remarkable constancy of internal physico-chemical conditions during the life of the animal. It appears justifiable again to call attention to some of these facts with a brief description of some of the mechanisms involved in order better to emphasize some of the interpretations of, and inferences drawn from, them in so far

[11] Reichert, *Science*, 1914, N. S., XI, pp. 649–661.

as these interpretations and inferences have to do with the general problem of evolution. We may, then, first of all briefly review the more salient of these facts, and afterward attempt their interpretation in terms of well-known physico-chemical laws—*e. g.*, the law of mass action and the phase rule.

1. *Thermo-Regulation in the Higher Organisms*

We may divide the vertebrates into two general groups on the basis of their internal or body temperature; (1) those which maintain a relatively constant internal temperature and (2) those whose internal temperature is variable. These groups may be tabulated as follows:[12]

TABLE I

I. Animals with a constant body temperature.		
	Adults or partly grown mammals and birds	about 42° C. or 107° F. Birds. about 39° C. or 102° F. Mammals. about 37° C. or 98.6° F. Man.
II. Animals with an inconstant body temperature.		
	(*a*) Animals which die when the temperature falls below 20° C.	Newborn mammals and birds.
	(*b*) Animals which become torpid when the temperature falls below 20° C.	Hibernating forms—some mammals.
	(*c*) Animals which remain active when the temperature falls below 20° C.	Reptiles, batrachians, fishes, among vertebrates; molluscs, insects, and the invertebrates generally.

Looking now to the differences between lower and higher vertebrates, to restrict ourselves at the start to a relatively small part of the animal kingdom, one of the most noticeable changes has been the development of a very constant body temperature in the so-called warm-blooded or homoiothermal animals (Table II). The detailed enumeration of the body temperature of all the animals so far observed would require too much space, but the following data will be sufficient to show upon what basis of fact the statements rest:

[12] Richet, Dictionnaire de Physiologie, 1898, t. III, pp. 85–86.

TABLE II

TABLES OF BODY TEMPERATURE

1. *Birds*

Genus or Species	No. of Observations	Temperature		Observer
Sparrow	1		42.1° C.	Davy.
Turkey	1		42.7	Davy.
Peacock	1	40.5 to	43.0	Davy.
Guinea fowl	1		43.0	Davy.
Duck, domestic	110	(Mean)	42.07	Martins.
Anas	179	(Mean)	42.3	Martins.
Anas		(Maximal)	43.45	Martins.
Anas		(Minimum)	40.8	Martins.
Palmipeds, divers	9		40.6	Davy, Eydoux, Brown-Sequard, Souleyet.
longipennes	69		40.6	
Pheasant	5		42.5	Richet.
Hen	17		42.5	Mantegazza, Demarquay, Dumeril, Davy, Prevost and Dumas.
Pigeon	600	(Mean)	41.9	Chossat.
		(Noon)	42.22	
		(Midnight)	41.48	
Pigeon	10	(Mean)	41.2	Corin, Van Beneden.
		(Maximum)	43.6	
		(Minimum)	39.	Daily variation 2.2
Pigeon	31	(Mean)	41.8	Zander.
		(Maximum)	44.	
General mean			42.0	

Richet[13] considers it probable that the temperature of birds is always above 40° and never, except under extreme conditions, above 44° C.

Further measurements are given by Sutherland Simpson.[14]

2. *Mammals*[15]

Genus or Species.	Temperature.
Pigs	39.7° C.
Sheep	39.6
Oxen	39.5
Rabbits	39.5
Dogs	39.2
Guinea-pigs	39.2
Monkeys	38.3
Horses	37.7
Monotremes	30.0

[13] Richet, *loc. cit.*, p. 87.

[14] *Proceedings of the Royal Society of Edinburgh*, 1911–12, XXXII, pp. 19–35.

[15] Richet, *loc. cit.*, t. III, p. 91.

The monotremes occupy a peculiar position in the scale (Table III). Their internal temperature, while relatively constant and considerably above that of the external air, is notably lower than that of mammals generally.[16] This group probably presents a transition stage between the poikilothermal animals and the homoiothermal animals with a higher body temperature.

TABLE III

SHOWING BODY TEMPERATURE OF THE MONOTREMES

	Temperature		
	Cloacal	Peritoneal	External
Echidna aculeata, var. typ.	26.5° C.	29.0° C.	21.5° C.
Echidna aculeata, var. typ.	29.5	31.5	22.0
Echidna aculeata, var. typ.	30.5	31.5	18.0
Echidna aculeata, var. typ.	31.5	31.5	18.0
Echidna aculeata, var. typ. young	31.0	31.5	24.0
Echidna aculeata, var. typ. young	34.2	31.5	22.5
Echidna aculeata, var. typ.	34.0	36.0	31.5
Echidna aculeata, var. typ.	28.3	30.0	31.5
Echidna aculeata, var. typ.	28.3	26.9	20.0
Ornithorhynchus paradoxus	24.4	26.9	20.0
Ornithorhynchus paradoxus	25.2	25.2	23.0

The normal diurnal variation in temperature of the human has been studied by many observers. The temperature varies not only with the time of day, but with the taking of food, with age, with external temperature and with other conditions to which we will return later. On the average, the highest temperature is attained in the evening between five and eight o'clock, and the lowest in the early morning between two and six, with upper and lower limits of 37.5° C. (99.5° F.) and 36.3° C. (97.4° F.), respectively. The body temperature may, of course, be greater or less without any necessary implication of disease processes, but the figures given may be considered as fairly representative.[17] It seems well established that, in conditions of health, the daily variation in temperature is about one per cent. of the mean—98.4° F.—expressed in the Fahrenheit scale. It is a peculiar fact also that the

[16] Richet, p. 90, Table II, and C. J. Martin, *Philosophical Transactions of the Royal Society*, London, 1903, Series B, Vol. CXCV, p. 1.

[17] Stewart, "Manual of Physiology," 6th ed., New York, 1910, p. 605.

normal body temperature is fairly close to the upper limits of body temperature compatible with life. A variation of five per cent. from the mean, expressed in degrees Fahrenheit, is often cause for grave anxiety, and a variation of ten per cent. is usually fatal. Compared with this, the variation in body temperature of fishes which live in the water only a few degrees above the freezing point in the winter and in the tepid water of a shallow stream in the summer is enormous.

The highest temperatures recorded in the human, after which recovery has occurred, are shown in Table IV.

TABLE IV

Temperature	Disease Suffered	Observer
43° C.	Hystero-epilepsy	Miersejewski, cited by Lombroso.
42	Typhoid fever	Alvarenga.
42.3	Scarlatina	Bouveret.
43.6	Scarlatina	Vicente et Bloch.
42.2	Periostitis and pyemia	Weber.
43.3	Intermittent fever	Mader, cited by Seguin.
44	Intermittent fever	Hirtz.
44	Intermittent fever	Alvarenga.
44.6	Intermittent fever	Riess.
46	Intermittent fever	Bassanovitz.
46	Intermittent fever	Diez Obelar.
46	Intermittent fever	Capparelli, cited by Richet.
44.8	Intermittent fever	Whitney.
43.3	Rheumatism	Wilson Fox, cited by Seguin.
44.9	Hysterical icterus	Lorentzen.
44	Hysteria	Clemow, cited by Gilles de la Tourette.
45	Hysteria	Lombroso.
45	Hysteria	R. Visioli.
43.6	Hysteria	Sciamanna.
43.9	Fracture of the cervical vertebra	Brodie. Lorain.
44	Fracture of the 12th dorsal vertebra and delirium tremens	Simon.
43.8	Fracture of the 6th cervical (19 hours after traumatism)	Frerichs.

The somewhat alarming but relatively innocuous manifestations of hysteria are attended by a high temperature without the complicating factor of an infection, and pres-

ent, therefore, the effects of temperature alone. It will be noted that the body temperature attained in hysteria—45° C. or 113° F.—and 46° C. in a case of intermittent fever with recovery is nearly as high as we have found recorded—45.7° C. or 114.3° F. after death in a case of tetanus, and is next to the highest recorded, as far as our observation goes, with recovery of the patient. The temperature of the body may, however, rise still higher under the influence of external agents. Thus, in death from strong electric currents, Klein[18] reports a body temperature of 132° Fahrenheit (55.5° C.) or even 140° F. (60° C.) immediately after death.

The effect of temperature upon the contractile manifestations of protoplasm has been summarized by Schäfer:[19]

> In warm-blooded animals the phenomena cease altogether to be exhibited if the protoplasm which is under observation is cooled to below a temperature of about 10° C., although they will be resumed on warming the preparation again, and this even if it has been cooled to 0° C., or a little lower. And when warmed gradually, it is found that the movements become more active as the temperature rises, attaining a maximum of activity a few degrees above the natural temperature of the body, although if maintained at an abnormally high temperature they are not long continued. A temperature a little above this maximum rapidly kills protoplasm, at least that of vertebrates, producing a stiffness or coagulation in it (heat-rigor), which is preceded by a general contraction; from this condition of rigor the protoplasm can not be recovered. But the protoplasm of some organisms will stand temperatures approaching that of boiling water without passing into heat-rigor. Freezing may cause destruction of protoplasm in higher animals, but that of certain of the lower animal and plant organisms is capable of resisting extreme cold, apparently for an indefinite time. This has also been found true for seeds of plants (Dewar).

Frog's muscle (gastrocnemius) reaches its maximum efficiency at about 35° C., after which a falling off occurs as the temperature is increased. Heat-rigor makes its appearance at about 41° C.—about two degrees Centigrade above the usual body temperature of a dog (an

[18] Klein, *New York Medical Journal*, May 30, 1914.

[19] Schäfer, "Text-Book of Microscopic Anatomy," London and New York, 1912, pp. 68–69.

average of 39.38° C. for 176 measurements), or slightly less than the usual body temperature of birds (42° C.).[20]

The maintenance of a constant temperature is dependent not upon one mechanism alone, but upon the coordinated interaction of several mechanisms. The presence of a coat of fur or feathers has long been recognized as a factor in maintaining the constant temperatures of mammals and birds. The development of such a protective covering has many times been emphasized by evolutionists, and seems to be well accounted for on the theory of natural selection. The fur or feathers tend to diminish heat loss from the surface of the body, but have nothing to do with the production or distribution of heat within the body. A subcutaneous layer of fat may still further reduce the heat loss from the surface, as in the Cetacea.

The production of heat is directly dependent upon oxidation in the muscles and glands of the body. A fall of general body temperature is attended by increased muscular activity, as shivering, when the temperature tends to fall unduly low. The muscular activity is dependent in its turn upon the nervous system, and upon the supply of oxygen and oxidizable substances through the blood.

The effect of the blood in maintaining a more nearly constant temperature of the muscles, as well as the production of heat by the muscles themselves, is shown by Meade Smith's experiments on mammalian muscles.[21] Although more heat is produced in a muscle which is contracting than in a resting muscle, there is still some heat production while at rest. When the artery going to a resting muscle was tied off, the difference in temperature between muscle and blood due to heat production in the muscle might be as much as 0.6° C. at the end of a five-minute period. When the circulation is intact, this difference in temperatures does not become so great. Tetanic stimulation of a muscle may lead to a considerable increase in the temperature of the venous blood coming

[20] Richet, "Dictionnaire de Physiologie," 1898, t. III, p. 86.

[21] Meade Smith, *Archiv für (Anatomie und) Physiologie* (Du Bois Reymond), Physiol. Abt., 1881, pp. 105–152.

directly from the muscle as compared with arterial blood.

The distribution of heat is accomplished by the circulating fluids of the body, and particularly by the blood. When the heat loss by radiation from the surface of the body becomes too rapid, the contraction of the walls of the peripheral blood vessels cuts down the quantity of blood going to the surface and, hence, the loss of heat as well. The constriction of the peripheral blood vessels and the contraction of the muscles tend to restrict the lower limit to which the body temperature may fall. The lower the external temperature, the greater the supply of heat from internal combustion needed to maintain the usual temperature of the body unless the radiation be checked by clothing or by artificial heat. It is generally stated that the temperature of the unclothed human body at rest may be maintained until the external temperature falls to 27° C. (Senator). This statement, as will be shown in a later paper, may be open to question. When the external temperature falls below this point, shivering or other involuntary muscular movement begins. This relation between temperature and metabolism accounts in large measure for the large amounts of food sometimes consumed by Eskimos. A young vigorous Eskimo may eat as much as four kilograms (nine pounds) of meat in a day.[22]

K. E. Ranke gives another illustration of the effect of climate upon diet in Germany and in Brazil. Allowing himself a free choice of food, the controlling influence being his appetite, his food requirements were 3,300 to 3,500 calories a day, when the external temperature range was from 15° C. to 22° C. In a dry atmosphere at 25° C., the fuel value of the diet fell to 2,800 calories. In an atmosphere with a temperature of 25° C. to 28° C. and a humidity of eighty-three per cent., the heat value of the diet fell to 1,970 calories in a day. This diet was insufficient

[22] Rink, cited by Lusk, "Fundamental Basis of Nutrition," New Haven, 1914, p. 28.

to maintain his body weight, and disturbances of his general health appeared.[23]

The cold-blooded and warm-blooded animals react differently to changes in external temperature. Thus, the carbon dioxide output of a frog rose from 0.015 gram per kilogram of body weight per hour when the external temperature was 1.6° C. to 0.639 gram when the external temperature was increased to 34° C. (H. Schultz). But as was first shown by Pflüger and his pupils, the metabolism of a warm-blooded animal increases as the external temperature is lowered. If, however, the body temperature is raised there is likewise an increase in the metabolism of the warm-blooded animals. Pflüger regarded the increase in metabolism of the warm-blooded animals accompanying the decrease of external temperature as a later acquisition or as a mechanism which has gradually been evolved in the special interest of a constant temperature. Rubner's measurements of the metabolism in a dog showed an increase from 30.8 calories an hour when the external temperature was 27.4° C. to 40.6 calories an hour when the external temperature was lowered to 11.8° C.,—an increase of about thirty-three per cent. These considerations are sufficient to suggest that the effect of similar changes in the environment may not only not have effects of equal magnitude upon organisms at different levels in the taxonomic scale, but may even have opposite effects at the two extremes of the scale.

The upward march of the body temperature is restricted by the greater access of blood to the periphery and the increased loss of heat by radiation from the surface. A still greater loss of heat, in addition to the rather constant amount lost by evaporation of water from the lungs, is brought about by evaporation of water from the skin or other surface of the body, such as the tongue in dogs. The amount of water on the skin is regulated by the activity of the sweat glands, and these, in their turn, are under nervous control.

[23] Tigerstedt, "Text-Book of Physiology," translated by Murlin, New York, 1906, p. 407.

Animals unable to maintain this constant body temperature throughout the year may maintain a constant temperature during the warmer seasons of the year and hibernate during the winter. This is particularly the case with small mammals, whose relatively large ratio of surface to mass may greatly facilitate heat loss, and with animals whose supply of food is difficult or impossible to obtain during the colder season. The body temperature of the animal falls greatly during hibernation. The importance of size in its relation to metabolism may be shown from the specific energy requirements of various animals. In general, the heat requirement of all well-nourished warm-blooded animals is about 35 calories per hour for each square meter of body surface. But since the surface varies as the square of the dimensions of the body, and the mass varies as the cube of these dimensions, the ratio of surface to mass is much greater in small animals than in large. A mouse requires 452 calories per kilogram of body weight in twenty-four hours, while a horse requires but 14.5 calories and a man about 24 calories in the same time.[24] To sustain a number of mice equal in weight to a man would require more than eighteen times as much food, measured in calories, as a man would need; and more than thirty horses could subsist upon the same amount of food that would be necessary to sustain a number of mice whose aggregate weight was equal to that of one horse. This is very different from saying how much food one mouse as large as a man or a horse would need, and should not, under any conditions, be confused with such a statement.

Milne-Edwards observed that in a small bird such as the sparrow, the body temperature might be lower in winter—40.8° C.—than in summer,—43.77° C.—the difference in temperature amounting to about 3° C.

The heat regulating mechanism of the body is, then, not a simple one but a complex one, involving muscle and gland, food supply and distribution of the blood, the nerv-

[24] Lusk, *loc. cit.*, p. 10.

ous system and the oxygen tension in the blood. We may next consider some of these subsidiary mechanisms.

2. *The Cardiac and Vascular Mechanisms*

The mechanism for the distribution of the blood is in itself a complex one, and involves (1) the mechanism controlling the rate and force of the heart beat and (2) the mechanism controlling the caliber of the blood vessels. When the cardio-regulatory and vasomotor nervous mechanisms are intact, a fall in blood pressure is attended by an increase in the rate of the heart beat; and, conversely, when the blood pressure tends to rise, the rate of the heart decreases. When the extrinsic nerves to the heart are cut, these changes in the pulse rate no longer occur as an accompaniment to the changes in blood pressure. The importance to the animal of these changes in heart rate with changes in blood pressure is shown by the fact that rabbits and dogs whose extrinsic cardiac nerves have been cut soon get out of breath on attempting to run.[25] Through the combined agencies of the vasomotor and the cardio-regulatory nervous mechanisms, the blood pressure in all mammals so far investigated[26] and in some birds, *e. g.*, ducks and fowls,[27] is very much the same, that is, about equal to a pressure of one hundred and twenty-five millimeters of mercury. Changes in the caliber of the blood vessels or in the rate of the heart beat equalize the local changes of pressure due to changes in muscular activity. Working glands or muscles receive, as a rule, more blood than similar organs at rest. This increase in blood-supply may be due in part to the action of metabolites upon the walls of the blood vessels of the active structure (Barcroft).

The blood pressure in the homoiothermal animals, or the blood pressure during the periods of activity of such

[25] See Guthrie and Pike, *American Journal of Physiology*, 1907, XVIII, pp. 27–28, for the earlier literature.

[26] Porter and Richardson, *American Journal of Physiology*, 1908, XXIII, p. 131.

[27] Riddle and Matthews, *American Journal of Physiology*, 1907, XIX, p. 108.

of them as hibernate, is significantly higher than in the poikilothermal animals. The precise significance of this higher pressure in the homoiothermal animals is unknown. It has been suggested that a certain pressure is necessary to overcome the friction of the blood against the walls of the blood vessels. It would appear that fully as much friction might be encountered in the vessels of a turtle weighing thirty or more kilograms as in the vessels of a guinea-pig weighing less than one kilogram. Yet the guinea-pig has the higher blood pressure. Nor does the difference in blood pressure appear wholly due to mere differences in viscosity of the blood of the two forms.

The general stages, from the point of view of function, in the phylogenetic development of the vascular system have been indicated elsewhere.[28]

In connection with the question of the rôle of a more or less constant blood pressure in the animal economy, we may mention the experiments of Legallois, Schiff and Goltz.[29] These investigators found that, while the cells of an animal do not die immediately after the blood pressure reaches a low level, the life of the cells in such an animal as the frog is not possible for indefinite periods of time, and in rabbits or dogs, death is a matter of hours. We may, perhaps, imagine that the low blood pressure may give rise to changes in the chemical systems in the cell that are incompatible with indefinite existence.

3. *The Respiratory Mechanism*

The respiratory movements in mammals, and probably also in birds, are, as Haldane and Lorraine Smith have shown, kept up at such a rate as will maintain a constant tension of carbon dioxide and oxygen in the alveoli of the lungs, and presumably in the blood leaving the lungs. The oxygen and carbon dioxide content of arterial blood may be supposed to be fairly constant in any one indi-

[28] Pike, *Quarterly Journal of Experimental Physiology*, 1913, VII, p. 23.

[29] The literature on the effects of low blood pressure has been given in the *American Journal of Physiology*, 1912, XXX, pp. 444–446.

vidual. The reaction of the body fluids is likewise dependent, in some degree at least, upon the tension of oxygen and carbon dioxide in the blood.

The reaction of the body fluids, particularly the blood, remains remarkably constant during the life of the animal. This is not so much the peculiarity of the higher organisms as is the constant temperature. The process of regulation of neutrality, as Henderson has shown, is a physico-chemical process and depends upon the properties of carbon dioxide, bicarbonates and phosphates in solution. The changes in concentration of hydrogen and hydroxyl ions in the blood are, in their turn, related to the respiratory rhythm.

The whole subject has been so well summarized by Haldane[30] that I venture to quote his statement entire.

> To illustrate this point I may perhaps refer to a subject which we have recently been investigating at Oxford. We have found that the respiratory center is so extremely sensitive to any increase or diminution of the partial pressure of carbon dioxide in the blood that a diminution of 0.2 per cent. of an atmosphere, or 1.5 mm. of mercury will cause apnea, while a corresponding increase will double the breathing. The recent researches of Hasselbach have afforded experimental evidence of what had already seemed very probable—that the stimulus to which the center responds is the difference in hydrogen ion concentration, or acidity, brought about by the very slight deficiency or excess of carbon dioxide. He has also investigated quantitatively the effect on the hydrogen ion concentration of the blood of varying the partial pressure of carbon dioxide. From his results and ours it follows that the hydrogen ion concentration of the blood during rest is extraordinarily constant, and remains so day by day and year by year. As the amount of acid and alkali passing into the blood from the food and other sources is constantly varying, it follows that the regulation of hydrogen ion concentration is mainly brought about by the kidneys. It has been known for long that the urine varies in acidity or alkalinity according to the diet; but Hasselbach has measured the actual variations in hydrogen ion concentration. Putting together his conclusions and ours, it appears that during ordinary resting conditions the variations in hydrogen ion concentration of the urine are about a hundred thousand times as great as those of the arterial blood.
>
> Thus the kidney epithelial cells react so delicately to variations in

[30] Haldane, "Mechanism, Life and Personality," New York, 1914, pp. 49–51.

hydrogen ion concentration of the blood, that the very smallest variation in the direction of acidity or alkalinity excites them to excrete a liquid which is, relatively speaking, intensely acid or alkaline, the net result being that the normal hydrogen ion concentration of the blood remains practically constant.

When we have such figures before us we realize the marvellous fineness of the regulation by the kidneys and respiratory center. Physiologists are still so much under the influence of the old gross mechanical theories of secretion that attempts at exact measurements of the delicacy of regulation by the kidneys have hitherto scarcely been made in the case of regulation in other directions, though we have every reason to believe that similar delicacy exists as regards the regulation of the water, salts, and other blood constituents. It is hard to realize that something which looks under the microscope like nothing more than a somewhat indefinite collection of gelatinous material can react, and continue throughout life to react, true as the finest mechanism of highly tempered steel, to the minutest change in its environment.

TABLE V

SOLUBILITY OF GASES IN WATER; VARIATION WITH THE TEMPERATURE

The table gives the weight in grams of the gas which will be absorbed in 1000 grams of water when the partial pressure of the gas plus the vapor pressure of the liquid at the given temperature equals 760 mm.

Gas	8° C.	10° C.	20° C.	30° C.	40° C.	50° C.
O_2.....	.0705	.0551	.0443	.0368	.0311	.0263
H_2.....	.00192	.00174	.00160	.00147	.00138	.00129
N_2.....	.0293	.0230	.0189	.0161	.0139	.0121
Br_2.....	431.	248.	148.	94.	62.	40.
Cl_2.....	———	9.97	7.29	5.72	4.59	3.93
CO_2.....	3.35	2.32	1.69	1.26	0.97	0.76
H_2S.....	7.10	5.30	3.98	———	———	———
NH_3.....	987.	689.	535.	422.	———	———
SO_2.....	228.	162.	113.	78.	54.	———

Whether such a constant O_2 and CO_2 content of the blood of all poikilothermal animals is to be found under all conditions of existence is unknown, but the coefficients of absorption of oxygen and carbon dioxide at varying temperatures would indicate that the carbon dioxide and oxygen held in solution in the body fluids would be subject to change with a change in temperature.[31] In the higher forms, the iron-bearing respiratory pigment, hemoglobin, absorbs all the oxygen with which it combines

[31] Table V, from Table No. 130, p. 142, Smithsonian Physical Tables.

within wide ranges of barometric pressure. There is some difference in the processes of absorption at high and low barometric pressures (Haldane), but the end result is essentially the same. No more oxygen is taken up by the hemoglobin at pressures of two or three atmospheres than at a pressure of half an atmosphere although the amount of oxygen dissolved in the fluid portion of the blood may be greater at the higher pressures. This difference is insignificant compared with the total oxygen in the blood. In the lower forms, manganese in the Echinoderms, and copper in certain Crustaceæ take the place of the iron in the respiratory pigment. The general conditions under which the oxygen is carried in the blood are, however, essentially the same in the various forms.

4. *The Concentration of Sugar in the Blood*

It has been stated since the time of Claude Bernard that the blood in the portal vein at the height of digestion contains more sugar in unit volume than the blood in the hepatic vein. The liver of the homoiothermal animals converts sugar to glycogen and stores it up in that form. Further extensive storage of glycogen occurs in the muscles.

While, under ordinary circumstances, there is good reason to believe that the concentration of sugar in the blood of a given animal is fairly constant for a given set of conditions, it is known that the amounts of sugar in the blood may vary under other conditions. Excessive amounts of sugar in the blood are eliminated by the kidneys. If the concentration of sugar falls, the transformation of glycogen to sugar makes up the deficiency. The concentration of sugar in the blood is not necessarily the same for any two species of animals under essentially the same conditions. Nor does the concentration of the sugar in the blood remain constant in any one individual, cat, dog, or human, under all conditions.[32]

[32] Cannon, *American Journal of Physiology*, 1914, XXXIII, p. 257; Scott, Ibid., 1914, XXXIV, p. 271; Shaffer, *Journal of Biological Chemistry*, 1914, XIX, p. 297.

It is probable that an organ or organs having a glycogenic function exist in some invertebrates, *e. g.*, the oyster, since glycogen may be obtained from these animals. Whether such a delicate adjustment similar to that obtaining in the higher animals between stored glycogen and circulating carbohydrate exists in these forms is unknown to us.

5. *The Osmotic Pressure of the Body Fluids*

In many species of homoiothermal animals, the osmotic pressure of the blood, as measured by the depression of the freezing point, is very constant, nor can it be easily influenced by changes in the environment. The ingestion of large quantities of water may be followed by the secretion of large quantities of dilute urine or by profuse perspiration. A shortage of water to drink leads to the secretion of small quantities of more concentrated urine. Both qualitatively and quantitatively, the physico-chemical constitution of the blood varies within relatively narrow limits.

6. *The Digestive Tract*

The mechanical and chemical processes of the alimentary tract reduce all the food, or its digestible portions, to water-soluble substances, in which form they are absorbed. The proteins of the food are reduced to the amino acids or polypeptids, the starches and sugars to monosaccharides and the fats to soaps before being absorbed.

The introduction of foreign proteins, *e. g.*, egg albumen, as such directly into the blood of the host is injurious. But the amino acids and polypeptids to which this protein is hydrolyzed by the action of the digestive enzymes are, in general, qualitatively the same as those in the blood of the host. The difference in proteins depends upon the difference in the quantitative relations of the amino acids in the protein molecule as well as upon the qualitative differences. The hydrolysis of all proteins to their

simpler splitting before absorption is a mechanism of protection against the entrance of foreign protein into the blood.

The alimentary tract to a certain extent renders the individual independent of the quantitative or stereochemical constitution of the proteins of its food, the only necessity being the presence of certain amino acids in the food.

But efficient as the alimentary tract is, it does not exclude all foreign or inutilizable substances. Cholohematin for example, from sheeps' bile, characterized by a peculiar spectrum and hence susceptible of easy identification, is absorbed by the dog and at least some of it is excreted in the dogs' bile without change.

The protection due to changes in the mucous membrane of the alimentary tract is well shown in the case of arsenic. It was long supposed that the arsenic-eating peasants of the Austrian Tyrol had become immune to the effects of a considerable concentration of arsenic in the blood, since they were able to take large quantities of it by mouth without suffering the usual effects of an overdose. It was shown by Cloetta[33] that the apparent immunity arose from changes in the intestinal mucosa which prevented the absorption of all but a small percentage of the arsenic taken.

If the lower members of the fatty acid series be fed to a dog the body fat which is stored up is softer and of a lower melting point than usual. Excess fat in the food may be stored up as body fat, but under certain conditions, the animal may use as much fat as is taken in the food, and the animal remains in metabolic equilibrium so far as the fat is concerned.

Although the amount of protein necessary to sustain life in an adult or to provide for growth in a young animal varies with the nature of the protein taken in the food, the animal is able to build up its own body protein from

[33] Cloetta, *Archiv für Experimentelle Pathologie und Pharmakologie*, 1906, LIV, p. 196.

any food which contains the requisite amino acids. The power of synthesis of new amino acids in the body is limited. Glycocoll, for example (amino-acetic acid), may be synthesized in the body. More protein is needed as food if its content in certain of the amino acids is low than if its content of these necessary acids is high.[34] But under all the varying conditions, within wide limits, the animal may maintain itself in nitrogen equilibrium, neither storing up any nitrogen in its flesh nor losing any from its tissues. The excess of any particular amino acid above that necessary for tissue growth or repair is eliminated from the body. Voit's famous 35 kilo dog was able to maintain nitrogen equilibrium when fed on amounts of protein varying from 480 grams of meat a day as a lower limit up to 2,500 grams a day.

The quantities of fluid, fat and protein in the blood, while undergoing some changes with the varying conditions of nutrition, starvation and fasting, remain close to a standard concentration as long as life lasts. Variations of great magnitude are incompatible with the prolonged life of the organism.

7. *Epidermis and Other Protective Mechanisms*

In addition to absorption, the limiting membranes of the body have other and important functions. The entrance of many harmful foreign substances into the organism is prevented by the protecting epidermis, the alveolar mucous membrane, and the intestinal mucosa, already noted.

But, however important the exclusion of harmful substances may be, the protection of the organism through the retention of valuable material is also of importance and must be provided for.

The escape of useful substances is prevented by the skin, the liver, the alimentary tract, the lungs and the kidneys. The splitting products of the hemoglobin arising from the death of the red blood cells are separated by

[34] Lusk, *loc. cit.*

the liver in the form of bile pigments, but the iron is conserved for use in the formation of new hemoglobin. But little iron is eliminated by the liver, although much iron may be stored there. The milk of higher animals contains but little iron, and the young mammal needs much iron for the formation of new blood cells during the rapid growth of early life. Provision is made for this by the storage of iron in the liver of the fetus. As postpartum growth proceeds, the amount of iron in the liver is reduced and the amount occurring in hemoglobin is increased.

8. *The Internal Secretions*

The internal secretions form another group of chemical conditions which vary within narrow limits in a state of health. Many years ago Caspar Friederich Wolff expressed the idea that each organ of the body stood in the relation of an organ of internal secretion to some other organ in the body. The liver liberates sugar which is necessary for the action of the muscles, and it also liberates urea which has a definite relation to the action of the kidneys. The muscles set free carbon dioxide which acts upon a particular group of cells in the nervous system, and nitrogenous waste products, some of which are transformed to urea in the liver. But apart from these more general relationships, a system of ductless glands sets free a variety of chemical substances which bear a rather different relation to the development and activity of many other organs and tissues of the body.[35] The relation of the adrenal gland to the myo-neural junction of sympathetic and smooth muscle fiber[36] is well known. The dependence of the development of the secondary sexual characters upon the internal secretion of the sexual glands is also familiar to biologists. The internal secretions in general have become a part of the internal conditions of the organism and of the chemical environment of the cells of the organism.

[35] Mathews, *Science*, 1897, N. S., V, pp. 683–685.

[36] Elliott, *Journal of Physiology*, 1905, XXXII, p. 401.

9. *The Mechanisms for Elimination of Waste Products*

The elimination of waste products occurs promptly and surely. The liver of higher animals not only separates out the useless portions of the hemoglobin derived from worn-out corpuscles (with retention of the iron-bearing part), in the form of bile pigment, but also transforms the ammonia compounds arising from nitrogenous metabolism to the relatively non-poisonous urea. The known chemical functions of the liver[37] are numerous. The kidneys promptly remove the urea and uric acid from the blood as these and other products of metabolism accumulate following activity of the cells. Certain mineral salts, *e. g.*, iron, are excreted by the intestinal mucosa. Some fat, in addition to that which is not absorbed from the food, is also excreted from the intestine.

The attempt to tabulate the various excretions of the body reveals the fact that, although the qualitative composition of the bile and the urine is relatively constant, the quantitative variations are very wide under different conditions. The quantity of carbon dioxide exhaled during twenty-four hours depends upon the diet and upon the amount of muscular activity during the day. Although somewhat disconcerting at first sight, in view of the constancy of internal conditions, this very inconstancy of the excretions is to be regarded as a consequence of the maintenance of constant internal conditions. For it is only by the conservation of those necessary elements or substances whose supply is limited, and the free elimination of waste products or of other substances in excess that the constancy of internal conditions can be maintained. Intake and outgo of matter and energy are such as to maintain relatively constant physico-chemical conditions within the organism. The greater the energy requirements of the organism, the greater must be the intake to meet these requirements, and the greater the amount of waste products eliminated.

[37] Hofmeister, "Chemische Organization der Zelle," ein Vortrag; Braunschweig, 1901.

The list of mechanisms, organs and tissues of the animal body and of specific organic or inorganic substances within the body, whose conditions and concentration remain relatively constant, could be extended. The description of these phenomena bulks large in the extensive literature of physiology of to-day. Sufficient data have been adduced to show that there is a considerable basis of fact for the interpretations which we now wish to present. A summary of the known facts of the internal conditions of the organisms permits of the statement that in the homoiothermal animals, there are, then, several mechanisms of extreme delicacy and great constancy under similar conditions and varying but little under wide changes of external conditions. The tracing out of their development constitutes a large part of the subject matter of comparative physiology. But their interpretation rather than their development is the thing of main interest at present. We will return to the questions of the origin and development of these mechanisms in later papers.

What point of view will give us the best insight into the rôle of these mechanisms in the evolution of the vertebrate phylum? Of what use have they been? Or are they simply mechanisms which have arisen in the course of evolution apparently through correlation with other phases of development but without obvious significance to the organism?

III. The Laws of Chemical Equilibrium

Before attempting the interpretation of these mechanisms, or pointing out their rôle in evolution, we may very briefly review the laws of chemical equilibrium as exemplified in the "slow" reactions of the physical chemist. For our present purpose, these laws may be included under the law of mass action, Van't Hoff's law and the phase rule. A fuller statement is given in Blackman's paper and in the text-books of physical chemistry.

1. *The Law of Mass Action*

The mass law or law of mass action expresses the relationship between the molecular concentration and the speed of the reaction. The concentration of the substance is usually expressed in terms of the number, either whole or partial, of gram molecular weights or gram molecules present in one liter of the solution. On the basis of Avogadro's law, there is the same number of molecules of sodium chloride in a gram molecule (58.4 grams) of sodium chloride as there are molecules of cane sugar in a gram molecule (342 grams) of cane sugar or molecules of oxygen in a gram molecule (32 grams) of oxygen. If equal fractions of the gram molecular weights of two different substances are each dissolved in a liter of water, there will be the same number of molecules in each of the two solutions.

Let two substances, A and B, be present in a solution in the concentrations (expressed in gram molecules) of c_A and c_B, respectively, at any stage of the reaction $A + B \rightarrow C + D$ and let the temperature remain constant throughout the action. The speed (S) of the forward action expressed in gram molecules of A and B transformed in unit time is defined by the relation $c_A \times c_B \times F = S$ where F is the affinity constant. As the reaction proceeds, c_A and c_B and, hence S, steadily decrease, since A and B are being continually used up. S may therefore be taken at any time as the quantity of A and B which would be transformed in the unit of time if the concentration c_A and c_B were maintained at a constant value by the continual addition of new substance. F is the measure of the intrinsic activity (affinity) which is the driving force in the reaction, and is independent of the concentration. If unit concentrations are taken, $c_A = c_B = 1$ and $F = S$. The activity, F, is thus represented numerically by the number of gram molecules transformed in unit of time when each reacting substance is present in unit concentra-

tion. Since c_A, c_B and S may be measured at any time, F may be calculated for any action.[38]

The law of molecular concentration or law of mass action is: In every chemical experiment, the speed of the action at any moment is proportional to the first, or some higher, power of the molecular concentration, at that time, of each interacting substance and to the intrinsic activity (affinity) of the substances.

2. *Van't Hoff's Law*

But the speed of any reaction at any concentration varies with the temperature. In general, the increase in speed is about ten per cent. for each increase of one degree Centigrade, or, as it is sometimes expressed, the speed of the reaction is doubled when the temperature is increased ten degrees Centigrade. This is known as Van't Hoff's law. The actual change in the speed of the reaction may be greater or less than ten per cent. for each change of one degree Centigrade, and is usually expressed by a coefficient. When the coefficient is 1.2 or less, that is, when the change in speed is two per cent. or less for each change of one degree Centigrade, the action is usually considered to be a physical and not a chemical action. When the temperature coefficient is greater than 1.2, the action is commonly considered to be a chemical action. No theoretical explanation of Van't Hoff's law of change in speed with change in temperature has so far been advanced.

These laws apply to reactions which go on at a measurable speed and which have been called "slow" reactions by the physical chemists. These "slow" reactions are to be distinguished from those reactions which proceed so rapidly that no measurement of their speed at different intervals is possible, or reactions of the explosive type.

[38] Smith, "General Inorganic Chemistry," 1st ed., New York, 1906, p. 251.

3. *The Phase Rule*

One other principle of physical chemistry finds frequent application in biology, and that is the phase rule developed by Gibbs. The phase rule defines the condition of equilibrium existing in a system by the relation between the number of coexisting phases and components. "According to it a system made up of n components in $n+2$ phases can only exist when pressure, temperature and composition have definite fixed values; a system of n components in $n+1$ phases can exist so long as only one of the factors varies and a system of n components in n phases can exist while two of the factors vary. In other words, the degree of freedom is expressed by the equation

$$P+F=C+2, \text{ or } F=C+2-P,$$

where P designates the number of phases, C the number of components, and F the degree of freedom."[39] In other words, F represents the number of conditions which may be varied without causing one of the phases to disappear.

An example of the phase rule, based upon the properties of a familiar substance, is that of ice, liquid water and water vapor existing together in a closed vessel from which the air has been exhausted. Ice, liquid water and water vapor each constitute a phase of the system, and there is but one component or substance—water—present. Here, one component exists in three different phases. We have, then, n components and $n+2$ phases. The essential conditions for the existence of the system are temperature and pressure of the water vapor. In the notation quoted above, $P=3$, $C=1$. Hence, $F=1+2-3=0$. Neither of the conditions—temperature or pressure—of the system can be changed without causing one of the phases to disappear. There is no degree of freedom, or, as it is sometimes expressed, the system is a non-variant system. The exact conditions for stability

[39] Morgan, "Physical Chemistry," New York, 1911, p. 119.

of such a system are a pressure of water vapor equal to 4 mm. of mercury and a temperature of .007° C. above 0° C.—the freezing point at atmospheric pressure.

Many applications of the phase rule to living matter have been made. We will cite but one. The globulins—typical proteins found in the blood of animals—are insoluble in distilled water, but are soluble in dilute solutions of the inorganic salts, such as sodium chloride. The globulin may exist in a system of water, sodium chloride and globulin, as globulin in solution or as precipitated globulin. The globulin is the only component existing in more than one phase under the conditions of the experiment.[39a] Addition of water to the system to such a degree that the concentration of the inorganic salts falls below a certain minimum leads to a precipitation of part of the globulin in solution. The removal of the mineral salts, keeping the volume of the solution constant, will also lead to precipitation wholly or in part, of the globulin in solution. But whether water be added or salt removed, the essential condition which undergoes changes is the concentration of the salt. Pressure does not enter in as one of the conditions of the system. And if the temperature of the system be raised above a certain point, depending upon the globulin present in the system, the globulin will be precipitated. In this system, the number of components is one (globulin) and the number of phases is also one, dissolved globulin. We have, therefore, a system of n components with n phases, and two of the conditions may vary, within certain limits, at the same time, viz., the concentration of the sodium chloride and the temperature. In the terminology of the quotation above, $P=1$, $C=1$ and $F=1+2-1$, or 2. This is also expressed by saying that the system is divariant. This system is of interest because of the fact that it also illustrates the phenomena of maximum points.

[39a] While globulin is not the only component entering into the system, we have restricted the discussion to the department of the globulin for reasons of space and simplicity.

Further details should be sought in the text-books of physical chemistry, and especially those by Bancroft and Findlay on the phase rule.[40]

IV. The Interpretation of the Regulatory Mechanisms in Terms of Chemical Equilibrium

But what evidence is there that the laws of mass action or of chemical equilibrium apply to living matter? Is there any evidence that the reactions occurring in the cell are "slow" reactions similar to those of the physico-chemical laboratory? The answer to these questions is decidedly in the affirmative. Much evidence in favor of such a view was presented by Blackman. Hofmeister, Bredig and others regard the cell as a congeries of enzymes, each one, according to Hofmeister,[41] acting in its own compartment upon its own peculiar substrate.

1. *Applications of Van't Hoff's Law*

As further evidence of the nature of the reactions in living matter, we may cite the work of Shelford[42] on tiger beetles, in which the length of the combined quiescent periods of the pupal and the prepupal stages was increased from four or six weeks at a temperature of 28° to 30° C. to ten or twelve weeks at a temperature of 15° to 17° C. Riddle[43] found that the temperature coefficients for digestion in *Amia, Rana, Necturus* and the common turtle (*Emydoidea*) ranged from 0.93 in *Necturus* to 7.81 in the turtle. Rogers and Lewis[44] have recently shown that the temperature coefficient of the rate of contraction of the dorsal blood vessel of the earthworm is of the order of magnitude to be expected if the processes

[40] Bancroft, "The Phase Rule," Ithaca, New York; Findlay, "The Phase Rule and Its Applications," 3d ed., 1911, London and New York.

[41] Hofmeister, *loc. cit.*

[42] Shelford, *Linnean Society's Journal*, 1908, XXX, p. 176.

[43] Riddle, *American Journal of Physiology*, 1909, XXIV, pp. 447–458.

[44] Rogers and Lewis, *Biological Bulletin*, 1914, XXVII, p. 269. See also Lehenbauer, "Physiological Researches," 1914, I, pp. 247–288.

concerned are of the nature of slow chemical reactions. The application of Van't Hoff's law in these instances is sufficiently plain.

Considering the processes in living matter, from this point of view, we may gain some insight into the reason why so many of the factors or conditions entering into the reactions occurring in the body of a higher organism should be kept as nearly constant as possible.

2. *The General Conditions of the Reactions in the Cells*

In determining the velocity of a reaction, we may determine (1) what quantity of the reacting substances combine or react in unit time, the usual method of the laboratory, as has been shown above, or (2) we may determine what quantities of material must be added in unit time to keep the reaction going at a constant rate. Recalling now the nearly constant factors in the higher mammalian organism, the oxygen content, the temperature, and the hydrogen ion concentration all varying within relatively narrow limits, and the variations usually being in such a direction as to get more material to an active or working structure in unit time, we can see that there are certain very effective devices for maintaining a reaction at a constant speed, which are the counterparts of the apparatus employed in the chemical laboratory. But the mechanisms in the living organism are capable of regulating, with a great degree of exactness, more conditions than any artificial mechanisms so far devised in the laboratory can control.

In the evolution of the organism the development of the various regulating mechanisms which we have described has brought about a set of conditions which tend to keep the environment surrounding the cells relatively constant. The analogy beween the reactions in the cells and the slow reactions of the physical chemist becomes clear. The temperature of the body being constant, the reactions in the cells, dependent as they are, upon a constant supply of material, go on at a relatively constant rate, or at such a rate as is determined by the needs of

the organism, and a rate which is provided for by the changing distribution of the blood.

Not all the physico-chemical conditions of cell activity are as constant as those discussed in the second division of this paper. Nor does the experimental interference with certain body structures leading to known departures from the usual conditions always entail serious results. As an instance of this we may cite the experiments of Ogata,[45] who investigated the rate of absorption of protein when fed by the mouth as compared with its rate of absorption when introduced directly into the intestine through a fistula. Taking the nitrogen output in the urine as the expression of the rate of absorption, the nitrogen output rose much more rapidly after direct introduction of the meat into the intestine than it did when the meat was fed by mouth. Although the absorption of the food was apparently more rapid than usual, the capacity for adjustment on the part of the organism was not exceeded. We may mention in passing that one function of the stomach may be to act as a storehouse and provide for a more gradual absorption of food than would otherwise occur. In the terminology of this paper, there is a less sudden entrance of constituents tending toward a disturbance of the equilibrium when the stomach is present than when it is absent. If food is administered in small portions and in a finely divided state after complete removal of the stomach, life goes on as usual (Czerny). But one is hardly justified in saying that, because great and profound changes do not occur in the organism after extirpation of the stomach, the stomach has no important function.

A detailed consideration of the inconstant or variable conditions and of the manner and extent to which changes in the environment can influence all internal conditions, must be deferred for another communication. Enough has been said in these pages to show, in outline at least, the essential uniformity of some important internal con-

[45] Ogata, *Archiv für Anatomie und Physiologie*, 1883, p. 89.

ditions of the higher organism and to indicate their rôle, on the assumption that the internal mechanisms of the organism are physico-chemical mechanisms.

In the response of the respiratory mechanism to the increased concentration of carbon dioxide or to lack of oxygen in the blood, we have an instance of adaptation which is not at once seen to be an obviously automatic and inevitable result of the physico-chemical properties of the environment. A striking characteristic of the respiratory center is at once its sensitiveness to slight changes in the concentration of carbon dioxide and its tolerance to the accumulation of carbon dioxide in the blood. The respiratory cells react to an extremely slight increase of carbon dioxide which is insufficient to affect the other cells, and remain sensitive to this increase after the concentration has risen so high that the visible responses of certain other cells have ceased. The common excitability of the respiratory and other motor nerve cells to carbon dioxide may be supposed to result from the disturbance or change produced in a complex system by the accumulation of one end product of the reaction, and to this extent to be an automatic result of the physico-chemical constitution of the cell.

The question raised by Mathison[46] as to whether carbon dioxide is a stimulant for all nerve cells is of interest in this connection. Carbon dioxide is certainly a stimulant for the central nerve cells of the respiratory mechanism, but it is not necessarily a stimulant to the same degree for all nerve cells. It is probable that all living matter is more or less sensitive to the accumulation of carbon dioxide since it is one of the waste products of all destructive metabolism. The cell bodies of the respiratory neurones, by reason of the development of this common property of excitability to carbon dioxide, have become especially adapted to respond to slight variations in carbon dioxide. The adaptation undoubtedly depends upon a physico-chemical change in the respiratory neu-

[46] *Journal of Physiology*, 1910, XLI, p. 448.

rones. The persistence of the common property accounts for the asphyxial convulsions of the spinal animals and for the movements which are sometimes considered to be respiratory movements and commonly attributed to so-called respiratory centers. But whether we consider that the cells of the respiratory group have gradually acquired a lower threshold value for stimulation by carbon dioxide than the other cells of the nervous system, or that the cells of the respiratory group have simply retained the the common excitability of protoplasm in general to carbon dioxide, and the remaining cells have undergone modifications which have raised their threshold value, makes little difference from the theoretical point of view. In an environment which is, so far as one can determine, uniform, certain quantitative variations have occurred which have resulted in a differential sensitiveness to carbon dioxide or to lack of oxygen. The changes have not been qualitative, since asphyxial convulsions involving muscles innervated from other parts of the central nervous system, may be brought on by a reduction of the oxygen supply.

The usefulness of the lower threshold value for lack of oxygen in a particular group of cells is at once apparent. Oxygen generation of the blood and elimination of carbon dioxide proceed without attention, and without noticeable excitation of any other group of nerve cells. There is no disturbance of the precision of movement of any group of muscles aside from those actually engaged in the respiratory act, nor the slightest effect upon the neurones involved in mental processes, resulting from the decreased oxygen or increased carbon dioxide tension in the blood sufficient to provoke a respiratory response.

3. *Stimulation in Terms of Chemical Equilibrium*

This brings us to a consideration of the nature of stimulation in general. Lack of space precludes all but the briefest mention at this time. We may here simply indicate the consideration in terms of the laws of mass

action and of the phase rule. That changes in the speed of reaction depend upon the concentration of the reacting substances or of the end products of the reaction has been shown in the discussion of the laws of mass action. It is not difficult to see that the respiratory movements owe their origin largely to changes in concentration of carbon dioxide and oxygen, and, since these changes result in a slight change in the concentration of the hydrogen ions it is not difficult to imagine that the law of mass action may be involved in the stimulation of the respiratory cells in the medulla oblongata. We have given in the third section of this paper two illustrations of conditions coming under the operation of the phase rule. It is true that living matter undoubtedly comprises vastly more complex systems than those described, but that the general principles underlying the reactions are similar in most important respects to the systems employed in laboratory experiments is scarcely to be doubted. The withdrawal of water from a cell or nerve fiber by osmosis or drying, entailing a quantitative change in the amount of water in the cell, is followed by other changes in the cell which tend to bring about a reestablishment of conditions in accordance with the laws of chemical equilibrium. That a change of phase of some of the components occurs in the process is probable.

Such influences as drying, applications of heat or mechanical pressure, whether occurring in the laboratory or in nature, are known as stimuli, and the changes associated with their operation in the organism are responses to stimulation. As Jost[47] has pointed out, the formal conditions of existence may act as stimuli to organisms. Although we must admit that a wide gap still exists, it seems to us that the discussion of stimuli and the processes of stimulation in terms of the law of mass action and the phase rule will enable us to meet in some degree, however small, Haldane's objection[48] that no causal con-

[47] Jost, "Pflanzenphysiologie," zweite Aufl., p. 618, Jena, 1908.

[48] Haldane, *loc. cit.*, p. 37.

nection has been shown between stimulus and response. And we may hope that here as elsewhere in biology the limits to our knowledge of nature will gradually be broken down.

The accumulation of waste products in the blood or body fluids through increase of their concentration in these fluids, leads to modified activity of the excretory and other organs. We cite a few examples.

The kidney, in addition to the elimination of water, follows the law of mass action in other ways. The volume of urinary secretion, other things being equal, is proportional to the volume of blood flow through the kidneys in unit time. The greater volume of blood carries with it a greater volume of waste products in unit time, and hence a greater volume of secretion is the result to be expected if urinary secretion is a physico-chemical process following the general provision of the mass law.

The accumulation of waste products arising from the slow reactions in the cells gives rise to the phenomena of fatigue, and the general slowing down of the cell processes, just as the accumulation of the end products of any slow reversible reaction decreases the amount of chemical transformation in unit time, in accordance with the mass law.

Excess of carbon dioxide, a typical waste product, even of the activity in nerves,[49] decreases or abolishes the conductivity of a nerve fiber. A stimulus (geotropic) may be applied to a plant in an oxygen-free atmosphere, but the responses will not occur until the plant is moved to an atmosphere containing oxygen.[50]

But even waste products in a certain concentration may be necessary for the optimum conditions of activity of an organ. Baglioni[51] points out that the selachian heart maintains its activity better in a solution of the inorganic salts containing two per cent. urea—the normal

[49] Tashiro, *American Journal of Physiology*, 1913, xxxii, p. 107.

[50] Jost, "Pflanzenphysiologie," zweite Aufl., p. 524, Jena, 1908.

[51] Baglioni, *Zeitschrift für allgemeine Physiologie*, 1906, VI, p. 71.

concentration of this substance in selachian blood—than in similar solutions without the urea.

V. General Considerations and Summary

The higher organisms have, therefore, developed a system of regulation by means of which internal conditions are kept relatively constant. This mechanism consists essentially of a physical means of distribution of material and heat—the circulatory organs and fluids—whose composition varies within narrow limits, a muscular, a glandular and a nervous mechanism for regulating the temperature, and a system of excretory organs for removing the waste products from the circulating fluids. Both chemical and nervous mechanisms of coordination are involved. The variations in the composition of the circulating fluids are such as will provide greater quantities of easily utilizable material at a time when it is needed. The internal secretions are important agents in maintaining the organism at a high pitch of efficiency through their influence upon the neuro-muscular apparatus and the general metabolism of all the tissues and organs. Regardless of the variations in external conditions, so long as these do not transcend the limits within which life is possible, and barring physical accidents or disease, the internal mechanisms keep it always fit, whether for work or rest, for battle or for play.

We have heard much about the survival of the fittest, and about the rôle of the strong jaw and powerful teeth and other physical characteristics in the struggle for existence. The doctrine of evolution, so far as its morphological side is concerned, may be regarded as fairly well founded. A little reflection, however, will show that the morphological aspect is only one phase of the problem. What profits it an animal to possess strong muscles and sharp teeth unless these muscles shall be at all times ready to contract quickly and surely? What if it become engaged in combat with an adversary and its muscles be

sluggish from cold? Or, supposing the temperature to be favorable, it be not able to control those muscles accurately and sink its teeth into the vital spot of the enemy? The answer is simple; another skeleton will soon lie bleaching. Somewhere or other evolution must have been concerned with the functional side. One protective mechanism has been suggested by the slow action of muscles in the cold and their more rapid action at higher temperature. The combat between a dog and a snake may be a fairly even one when the weather is warm, and very much in favor of the dog when the weather is cold. There is a strong presumption that the elaborate and complicated nervous vascular and glandular mechanisms, some or all of which are developed in birds and mammals, have some bearing on the general problem of evolution. It has rendered them far more independent of the environment than poikilothermal animals are. There is not so much necessity of hibernation during the winter, and a frosty morning is as good as any for hunting.

And if we consider that the changes of energy and material underlie all the other changes in the organism, regardless of the source from which they arise, it will be apparent that at least one part of the final discussion of evolution will be in terms of the changes of matter and energy within the organism.

The problems of the general processes of evolution—the adjustment of the animal to its environment or responses to changes in it, variation, adaptation, heredity and geographical distribution, and even the biochronic equation (De Vries) may all be approached from the point of view of the experimental physiologist. The consideration of these subjects will be taken up in subsequent papers.

CORRELATION BETWEEN EGG-LAYING ACTIVITY AND YELLOW PIGMENT IN THE DOMESTIC FOWL[1]

DR. A. F. BLAKESLEE AND D. E. WARNER

CONNECTICUT AGRICULTURAL COLLEGE

So far as the presence of visible yellow pigment is concerned, there are two groups of domestic fowls. In the first group, represented by the Orpington breed, yellow is constantly absent from legs, beak and body fat. In the second group, represented by the Leghorns and the so-called American breeds, such as the Plymouth Rocks, Wyandottes and Rhode Island Reds, yellow, in the form of yellow fat,[2] is present in varying amounts in the parts mentioned. In this latter group, individual birds may undergo considerable change in the amount of the yellow pigment visible. The standard of the show-room, however, demands yellow in the legs and beak in these breeds and, in consequence, birds that have become pale in these parts are liable to be scored down by the professional poultry judge. The paling or yellowing of the legs in the breeds mentioned has been attributed by poultrymen to various environmental factors. Thus, good health and vitality, abundance of range and exercise, proper food such as meat, corn, gluten meal and "green food" are said to increase the amount of yellow pigment, while poor health, moulting, confinement with insufficient exercise, running on sandy soil and in mud, as well as climate and the mere aging of the bird, are held to be responsible for the paling of the legs in these varieties.

Of recent years, some individual poultrymen have claimed that paling of the legs is due to heavy laying. This view has been maintained by J. E. Rice.[3] Mr. Tom Barron,[4] one of the most successful of the English poultrymen, in an address before the Connecticut Poultry

[1] Paper presented in brief before the American Society of Naturalists, Philadelphia, December 31, 1914.

[2] Barrows, H R., "Histological Basis of Shank Colors in Domestic Fowl," Bull. 232, Maine Agric. Exper. Station, 1914.

[3] Circular 54, N. Y. State Dept. of Agriculture, 1912.

[4] *Connecticut Farmer*, September 12, 1914.

Convention, July, 1914, described his use of the color of the legs in selecting high egg-producers. Moreover, the Maine Experiment Station, in a circular[5] which has come to our notice since the data in the present paper were obtained, advocates a similar use of the leg color in selecting hens for breeding.

The requirements of the "standard of perfection," which controls judging in the show room, as well as the common practice of poultry breeders, are opposed to a belief in any connection between laying and leg color. Woods,[6] under the title, "Has Leg Color Value Indicating Layers?", discusses the subject and concludes:

> Personally we believe that, as a practical guide in the selection of heavy layers or birds from which to breed heavy layers, the leg color, of itself, has no real value.

He further supports this conclusion by quotations from answers received from several prominent breeders to whom he had addressed a questionnaire on the subject.

So far as the writers are aware, no published data are available which show in how far the leg color may be of any value in selecting the laying hen, and such suggestions as have been made in this connection have confined themselves to a consideration of the legs alone. The results tabulated in the present paper show conclusively, it is believed, that a close connection does in fact exist between the yellow pigmentation in a hen and her previous egg-laying activity. They indicate further that the color of the beak is at least as distinctive as that of the legs heretofore alone considered in this connection, and that, in the Leghorns, the color of the ear-lobes is perhaps a better criterion of laying activity than either legs or beak and is more readily recorded.

The hens investigated were in the egg-laying contest located at Storrs, Conn. Pullets enter the contest November 1 and remain for one year. They are housed in pens of 10 birds each, are fed the same ration and so far as

[5] Circular 499, Maine Agric. Exper. Station. This is listed as an abstract of Bulletin 232.

[6] Woods, P. T., *Amer. Poultry Jour.*, p. 35, January, 1915.

possible are handled exactly alike.[7] The influence of different environmental factors, therefore, can be largely neglected.

A preliminary test was made the middle of last September by taking from each of a number of different pens a pair of birds representing the extremes of yellow pigmentation and comparing their egg records. This test indicated that the extremely pale birds were laying and the extremely yellow ones were not. It indicated also that the ear-lobes were much more easily graded as to color and in addition were apparently more indicative of egg-laying activity than the beaks and legs. The ear-lobes of the American breeds are red like the comb and wattles and do not show yellow pigment. The ear-lobes of certain other breeds, like the Blue Andalusians, are white but apparently remain without any appearance of yellow ever taking place. The Leghorns, including Browns, Blacks, Buffs and Whites, show marked changes in the amount of yellow in their ear-lobes. White Leghorns, of which there were over 300 in the contest, were accordingly chosen for closer study.

Ear-lobe Color in White Leghorns.—Color can be conveniently measured quantitatively by means of the Milton Bradley color top, which, when spinning, acts as a color mixer. In matching ear-lobes, only yellow and white sectors have been used. The matching is not perfect, especially in the lower grades, since a certain amount of bluish tinge is often present. The amount of yellow, however, has probably been more accurately measured than if the other color components were considered. By the method used, it appears possible under proper illumination for one to repeat readings with a change of seldom more than 5 per cent. yellow above or below the mean observation.

Top readings were taken of the White Leghorns listed

[7] Four pens of White Leghorns and four of White Rocks, belonging to the Experiment Station, had sour milk substituted for different ingredients of the normal ration, but, since they showed no apparent differences in color that could be attributed to the change in the feed, they were included in the tabulations.

TABLE I

AVERAGE EGG RECORDS FOR DIFFERENT AMOUNTS OF YELLOW IN EAR-LOBES OF 312 WHITE LEGHORNS

Per Cent. Yellow	No. of Hens	July	Aug.	Sept.	Oct	I Sept.	II Sept.	I Oct.	II Oct.	Year
5–10	7	23.1	21.3	19.7	15.3	9.9	9.9	9.29	6.00	197.1
11–15	36	21.8	22.1	18.2	14.2	9.4	8.8	8.14	6.03	187.9
16–20	40	22.2	20.7	16.9	11.7	8.8	8.2	7.50	4.17	184.3
21–25	16	19.8	21.4	16.4	8.1	8.1	8.3	5.56	2.50	164.3
26–30	20	19.5	18.9	10.3	3.2	5.5	4.8	2.75	0.45	148.5
31–35	31	18.0	17.7	5.5	0.5	3.5	2.1	0.45	0.00	139.1
36–40	33	19.7	17.3	6.1	0.2	4.2	1.9	0.15	0.00	139.6
41–45	41	18.2	16.2	4.9	0.2	3.4	1.6	0.22	0.00	134.2
46–50	39	18.0	15.6	4.0	0.2	2.6	1.4	0.18	0.05	138.2
51–55	30	18.4	16.1	3.6	0.1	2.9	0.7	0.00	0.07	137.8
56–60	13	14.8	10.7	2.4	0.0	2.2	0.2	0.00	0.00	124.7
61–65	4	14.5	8.8	1.3	0.3	0.3	1.0	0.25	0.00	100.8
66–70	1	3.0	0.0	0.0	0.0	0.0	0.0	0.00	0.00	70.0
71–75	1	0.0	0.0	0.0	0.0	0.0	0.0	0.00	0.00	83.0

TABLE II

PERCENTAGE OF HENS LAYING AND AVERAGE NUMBER OF DAYS SINCE LAYING FOR DIFFERENT AMOUNTS OF YELLOW IN EAR-LOBES

White Leghorns: total number of records, 932; total number of birds, 317

Per Cent. Yellow	5–10	11–15	16–20	21–25	26–30	31–35	36–40	41–45	46–50	51–55	56–60	61–65	66–70	71–75
No. records.....	41	125	80	67	62	92	94	94	108	84	44	28	9	4
Av. days since laying.....	0.4	1.6	7.3	17.1	26.2	37.9	41.5	44.0	45.1	51.3	55.9	61.4	50.3	71.0
No. records = laying.....	36	98	44	17	3	0	1	0	2	0	0	0	0	0
Per cent. records =laying.....	87.8	78.4	55.0	25.4	04.8	0	01.0	0	01.9	0	0	0	0	0

in Tables I and II at three different periods. The first recording took from October 7 to October 14, the second from October 19 to 21 and the last was completed in one day, October 28. The top records were all made by the same one of us (*B*), except for 197 records on October 28. The men who took these records had already acquired familiarity with the method, and while their readings are not absolutely comparable with the others, they probably are sufficiently so to be included in Table II. The three top readings were taken on separate sheets and the egg records were investigated after the readings were all taken and the birds had left the contest. Personal bias that might have influenced the readings was thereby avoided.

Table I shows the percentage of yellow in the ear-lobes

of 312 birds according to the records of October 19–21, together with monthly and yearly egg records for the different color groups. The months of October and September are each divided into halves. It will be seen that in general as the percentage of yellow increases, the egg production falls off, and that the correlation is most marked during the periods nearest the time when the records were taken. A distinct though slight correlation seems to show as far back even as July and is strikingly evident in the yearly averages. For months before September and October, the correlation with color is probably an indirect one. It is generally only the best birds—those that make the large yearly records—that are laying in October. Therefore, any method that selects the laying birds at this season will select, at the same time, the birds laying above average throughout the year and consequently give high yearly totals. It will be observed that 30 per cent. seems to be a critical amount of yellow. Above this amount comes the sudden drop in egg production for the months of September and October and also above 30 per cent. yellow the yearly totals fall to between 130 and 140, with but slight change thereafter.

In Table II, the records at the three different readings have been used. A bird laying on the day of record or on a later day within the month is considered to be laying and credited with a zero. If she laid on the day before the record but not later, she is credited with one "day since laying," and in a similar way a longer period of inactivity in laying is indicated by a larger number of days since laying. With the exception of a few cases where this was not possible, three records were taken of each bird. Since October is the season of decreasing egg production, the majority of the birds increased their quantum of yellow and consequently most birds are listed in more than a single color grade. Beginning with the 41 records in the 5–10 per cent. color grade which show an average of only 0.4 day since laying, the number of days increases consistently with the amount of yellow in the ear-lobes, the irregularity at 70 per cent. being probably due to the

smallness of the numbers in this group. The percentage of records that indicate actual laying drops rapidly from 87.8 per cent. for 5–10 per cent. yellow to zero for grades of yellow above 30 per cent.[8] The table shows that it is practically certain that a bird with an ear-lobe showing more than 30 per cent. yellow at the time of the records, is not in a laying condition.

TABLE III

AVERAGE EGG RECORDS FOR DIFFERENT GRADES OF YELLOW IN BEAKS AND LEGS OF 256 WHITE LEGHORNS

(P, M and Y are abbreviations for Pale, Medium and Yellow)

No. Birds	Beak	Legs	July	Aug.	Sept.	Oct.	I Sept.	II Sept.	I Oct.	II Oct.	Year
51	P	P	22.0	20.9	18.6	14.3	9.6	9.0	8.0	6.3	186.4
17	M	M	18.5	17.8	11.4	4.8	6.5	4.9	3.4	1.4	146.4
97	Y	Y	16.6	14.2	2.9	0.4	2.2	0.7	0.3	0.1	129.3
53	P	P 51 M 2 Y 0	22.1	21.0	18.3	14.0	9.4	8.8	7.9	6.1	185.3
43	M	P 25 M17 Y 1	20.1	20.6	13.7	5.7	7.4	6.3	4.2	1.5	164.6
160	Y	P 14 M49 Y 97	17.7	16.1	4.8	0.8	3.2	1.7	0.6	0.2	135.0
90	P 51 M25 Y 14	P	21.6	21.3	17.0	10.4	8.9	8.2	6.3	4.1	179.9
68	P 2 M17 Y 49	M	19.2	18.3	7.7	2.1	4.7	3.0	1.5	0.6	142.0
98	P 0 M 1 Y 97	Y	16.6	14.3	2.9	0.4	2.1	0.7	0.3	0.1	129.2
256	Averages of totals		19.0	17.8	9.1	4.3	5.2	3.9	2.7	1.6	150.4

Beak and Leg Color.—The beak and legs are more difficult to grade quantitatively than the ear-lobes. The color is less uniform in its distribution and has more of an orange hue, requiring the manipulation of at least one

[8] The three cases of laying, among the 557 records in the grades above 30 per cent. yellow were for sporadic layers. The one in the 40 per cent. group laid October 18, but at no other time in October or September. This case may perhaps be an error in the egg record. One of the two in the 50 per cent. grade laid during October only upon the 2d, 4th and 25th, though she laid 18 eggs in September; the other laid during October only on the 16th and 19th and had no eggs to her credit in the second half of September.

extra color disk in taking the records. A rough grouping by inspection into the three grades, *pale, medium* and *yellow,* however, gives a striking corroboration of the results obtained by the more accurate records on the ear-lobes and is applicable to breeds in which ear-lobe yellow is not present. The grading was always done by the same one of us (W.) who has had some familiarity in handling poultry. Probably no two observers would entirely agree in recording the colors but the difficulty comes in delimiting the grade *medium,* and not in deciding between the extremes, *pale* and *yellow.* The color records were taken on October 31 and November 1 to 4, as the birds were being packed for shipment and their egg records were looked up for tabulation after they had left the contest.

Table III corresponds to Table I. In the first three rows are listed the birds that agree in beak and leg color. In the second three rows the birds are grouped according to their beak colors without regard to their leg colors, while in the last three rows they are grouped according to leg color alone.

Table IV corresponds to Table II. Since egg records for these birds stopped on October 31, a bird laying on October 29 is counted among the layers even if she failed to lay on the 31st—the day she left the contest.

It will be noted from Table III that, in the Leghorns at least, where the numbers are large enough to make comparisons significant, the beaks, considered alone, seem to form a slightly better criterion for picking out the hens with high records, while the legs alone are better in selecting the poorest layers. In the great majority of cases in all the breeds considered, if the beak and the legs fail to agree in color it is the beak that is listed the yellower. In October the hens are falling off in laying and in consequence increasing in yellow pigment. Apparently the ear-lobes and beak are more quickly responsive to this change. In only 97 out of 160 Leghorns for which the beak was listed as yellow had the legs reached a similar grading in color.

Of the 51 White Leghorns listed in Table III as pale in

both legs and beak, 31 had ear-lobe records of 20 per cent. or less yellow on October 28. These averaged a yearly total of 191.9 eggs. The 40 birds of those in Table III that on this date had 20 per cent. or less yellow in ear-lobes, irrespective of the color of other parts, averaged a yearly total of 189.4 eggs. It appears therefore that hens with a higher yearly average may be obtained by selecting those that are pale in all parts—ear-lobes and beak as well as in legs—than if only one of these parts is considered.

TABLE IV

PERCENTAGE OF BIRDS LAYING, AVERAGE NUMBER OF DAYS SINCE LAYING AND YEARLY TOTALS FOR DIFFERENT COLOR GRADES OF BEAKS AND LEGS

(P, M and Y are abbreviations for Pale, Medium and Yellow; the color of beak is written first, followed by color of legs)

White Leghorns (256 birds with yearly average of 150.4 eggs)

	P.P.	M.M.	Y.Y.	P.M.	P.Y.	M. P.	M.Y.	Y.P.	Y.M.
No. birds	51	17	97	2	0	25	1	14	49
Av. days since laying	6.6	30.4	57.8	30.5	—	20.8	64.0	28.6	45.9
No. birds laying	32	2	1	0	—	3	0	1	1
Per cent. birds laying	62.8	11.8	1.0	0.0	—	12.0	0.0	7.2	2.0
Yearly averages	186.4	146.4	129.3	150.5	—	178.7	122.0	158.4	139.9

White, Buff and Columbian Wyandottes (79 birds with yearly average of 144.8 eggs)

	P.P.	M.M.	Y.Y.	P.M.	P.Y.	M.P.	M.Y.	Y.P.	Y.M.
No. birds	28	13	24	1	0	4	0	0	9
Av. days since laying	6.5	17.5	48.9	0	—	7	—	—	28.7
No. birds laying	16	5	0	1	—	2	—	—	1
Per cent. birds laying	57.2	38.5	0.0	100.0	—	50.0	—	—	11.1
Yearly averages	178.3	130.7	108.4	194.0	—	161.5	—	—	145.6

Barred, White and Buff Plymouth Rocks (82 birds with yearly average of 142.4 eggs)

	P.P.	M.M.	Y.Y.	P.M.	P.Y.	M.P.	M.Y.	Y.P.	Y.M.
No. birds	27	15	22	3	1	5	2	3	4
Av. days since laying	11.3	25.9	51.6	1.0	0.0	33.8	6.0	29.3	31.5
No. birds laying	15	3	0	2	1	0	1	1	3
Per cent. birds laying	55.5	20.0	0.0	66.6	100.0	0.0	50.0	33.3	75.0
Yearly averages	153.7	149.7	123.0	163.7	204.0	138.8	117.5	130.7	140.0

Rhode Island Reds (114 birds with yearly average of 128.8 eggs)

	P.P.	M.M.	Y.Y.	P.M.	P.Y.	M.P	M.Y.	Y.P.	Y.M.
No. birds	26	15	56	0	0	3	1	4	9
Av. days since laying	11.3	15.8	50.4	—	—	19.0	38.0	18.3	41.2
No. birds laying	14	7	2	—	—	0	0	1	1
Per cent. birds laying	53.9	46.7	3.6	—	—	0.0	0.0	2.5	1.1
Yearly averages	146.3	142.5	109.8	—	—	159.0	178.0	162.0	139.2

The method of grading beak and leg color may appear crude, but that it is capable of giving valuable evidence of previous laying activity is further shown by data kindly turned over to us by Professor C. A. Wheeler. On October 26, 1912, under his direction a series of measurements of 132 White Leghorns from the contest was taken by Mr. R. E. Jones. Among other records, the ear-lobes were graded as white, cream or yellow and the legs as pale or yellow, but no connection was worked out between the color and the egg records. These 132 birds we find to have a yearly average of 155.1 eggs. The 34 birds with pale legs averaged 188.9 eggs; the 98 with yellow legs, 143.5 eggs. The 33 birds with white lobes averaged 190.1, while the 99 with cream or yellow lobes averaged 143.5. The 21 birds that had both white ear-lobes and pale legs averaged exactly 200 eggs.

The data presented in the foregoing pages indicate a connection between the amount of yellow pigment showing in a hen and her previous laying activity. The most natural assumption is that laying removes yellow pigment with the yolks more rapidly than it can be replaced by the normal metabolism, and in consequence the ear-lobes, the beak and the legs become pale by this subtraction of pigment.

Environmental factors, other than laying, may be of more or less influence on yellow pigmentation. In fact, birds obviously sick have been observed to be pale although not in a laying condition. In the material investigated, however, variation in the laying activity seems to be the prime cause of the changes in yellow pigmentation in the domestic fowl.

The data of the present paper have been summarized in a preliminary report in *Science,* March 19, 1915. Photographs showing differences in yellow pigmentation in fowls are given in an article in the *Journal of Heredity,* April, 1915.

The change in yellow pigmentation is being further studied by a twice weekly top record of a flock of birds throughout the year.

SOME RECENT STUDIES ON FOSSIL AMPHIBIA

DR. ROY L. MOODIE

DEPARTMENT OF ANATOMY, UNIVERSITY OF ILLINOIS, CHICAGO

THE anatomy and relationships of the earliest air-breathing vertebrates have interested students of fossil animals so greatly since Georg Jaeger described the first Labyrinthodont in 1828, that the result to-day is a bibliographic list of over 600 titles, varying in importance from the magnificent work of Fritsch ("Fauna der Gaskohle") issued in four folio volumes with scores of lithographic plates, to short notices of a few lines. Many of the memoirs are handsomely illustrated and beautifully printed. The material so far described has been extremely fragmentary and the greater number of the contributions issued have been dedicated to the description of species based on incomplete material. The fauna was exceedingly diverse like the plesiosaurs of a later period, and new discoveries tend to confuse rather than to unify our ideas of amphibian morphology. The few papers reviewed below form no exception to the statement made above. Many new and importants facts are brought forth in the contributions made during the past few months and these are well worthy of consideration. Attention in these reviews will be paid especially to new facts of structural importance.

Broili (1) in a short paper has added to our knowledge of the Permian fauna of Texas by the description of two new species of Amphibia based on incomplete skulls. One of the species is very small, the skull measuring scarcely half an inch in length. The same writer (2) in a more extensive paper has given a popular review of the chief work done during the past ten years on the early air-breathing vertebrates and has listed the important papers from which he has used illustrations to elucidate his remarks. This paper should be consulted by any one who wishes a convenient and accurate survey of the earliest land vertebrates. Doctor Broili refers to *Micrerpeton*, the first branchiosaur known from the western hemi-

sphere, as a microsaur. The distinction between these two groups is clear, the former undoubtedly being ancestral to the modern Caudata and the latter having reptilian affinities. Likewise the author refers to *Lysorophus*[1] as a reptile, while the majority of paleontologists regard the form as Amphibian; Williston[1] even going so far as to locate it in the suborder Ichthyoidea of the Caudata. In conclusion Doctor Broili says:

> Im übrigen haben wir im Laufe der letzten 10 Jahre über die ältesten Tetrapoden so viel neues und wichtiges kennen gelernt, wie wohl in relativ keinem anderen Zweige der Wirbeltierpaläontologie. . . .

Broom (3) has given the results of his studies on Permian vertebrates in the American Museum. His reason for again describing and studying this much described and much studied material is that structural characters are difficult to determine in these forms on account of the very closely adherent matrix which has in many cases obscured all sutures in the skull. His discussion is accompanied by restorations of the skulls of the chief Permian genera, indicating most of the sutures, something which Cope was unable to do. He discusses some elements in the mandible not previously observed among Amphibia and suggests homologies between them and elements of the reptilian mandible. Unfortunately, Broom has paid no attention to the occurrence of lateral line canals on the skulls of these forms. It is highly important that this system of sense organs be distinctly understood. In view of Herrick's studies[2] on this structure in the catfish it is certain that this system of sensory organs has a distinct influence on the location of the peripheral osseous elements of the skull and mandible. I do not recall that Herrick's result have been noted by any paleontologist, but they should be taken into consideration. Broom says in regard to *Eryops*, the large Permian stegocephalian:

> . . . Every detail of the cranial structure can be clearly made out.

He criticizes Huene's (1913 *b*) work on the brain-case, however, and makes no statement concerning the lateral

[1] *Biol. Bull.*, Vol. XV, No. 5, p. 229, 1908.

[2] *Journ. Comp. Neurol.*, Vol. 11, p. 224, 1901.

line organs which were imperfectly studied some years ago[3] by the reviewer; so it is yet too soon to say that every detail of structure is known. The palate is very completely known and is figured by Broom. He has figured also very imperfectly, but for the first time, sections through the ear and brain-case showing the probable size of the dural cavity. He says that the portion of the paroccipital which lodges the labyrinth was cartilaginous, but does not give his reasons for this statement. In view of the almost perfect preservation of the semicircular canals in fishes, cotylosaurs and pterodactyls we should expect a favorably preserved specimen of an amphibian to show this structure also. He describes a pit in the basisphenoid for the reception of the hypophysis. He also figures for the first time the complete osteology of the mandible of *Eryops*. The author likewise describes and briefly figures two new species of stegocephalians. The same author (4) has given considerable attention to the study of the osteology of the mandible in *Trimeorohachis*, the discussion being very similar to that given in the above paper. The discussion has especially in view the problem of the derivation of the Amphibia from the Crossopterygia, and he figures the mandible, shoulder girdle and pectoral fin of *Sauripteris taylori* on account:

> . . . of (the) extreme interest from having the pectoral fin more closely resembling the tetrapod limb than in any other known form.

Case (5) reviewed before the American Paleontological Society the recent trend of studies on the air-breathing vertebrates of the Paleozoic. He states there are two general conclusions which have been reached by students of these early vertebrates. First, Baur initiated the idea of the crossopterygian ancestry of the Amphibia, and later workers have so far confirmed his suggestion as to make it extremely probably that the land vertebrates arose from these fishes. The intermediate stages are unknown. The second conclusion is

> that the primitive reptiles—the Cotylosauria—were derived directly from the Stegocephalia. . . .

So we are thus in possession of partial proof at least of

[3] *Journ. Morphol.*, 1908, Vol. XIX, p. 511.

the origin of reptiles from fishes through the Amphibia.

We owe to Doctor Fraas of Stuttgart many important contributions to the knowledge of the early air-breathing vertebrates and he has recently (6) issued another memoir on the labyrinthodonts of the Trias, the first study of these animals since the appearance of his large memoir in 1889.[4] The present contribution is devoted to discussions of new species and new facts concerning previously described species. The *Plagiosternum granulosum* is found to be the most peculiar labyrinthodont yet described, in that it is extremely frog-like in appearance, especially in the huge size of the orbits and the expanded occiput. It is interesting, furthermore, in the apparent absence or indistinct preservation of the lateral line canals. The photograph (Plate XVI, Fig. 1) of the dorsum shows portions of the supra- and infraorbital canals. The remainder of the cephalic system of sense organs was probably contained in pits, which, in the fossilized skull, are not to be distinguished from the ornamental scrobiculations of the membrane bones of the face. The auditory meatus is on the posterior edge of the skull and is quite large for the size of the skull. Doctor Fraas has given in a drawing (Plate XVI, Fig. 3) the complete osteology of the occiput of this unusual labyrinthodont. The remainder of the memoir is devoted to a discussion of new or disputed points in the osteology of various genera and species of Triassic labyrinthodonts.

Gregory (7) has reviewed the studies which have thrown light on the crossopterygian ancestry of the Amphibia, dealing especially with Watson's (11) recent paper on the Larger Coal Measures Amphibia, and giving a list of thirteen contributions which deal directly with this derivation of the Amphibia.

Huene (8) has again described the mandible of the peculiar Permian genus *Diplocaulus* although it has been many times studied, described and figured. He states, in his introductory paragraph:

> Gattungen, wie Diceratosaurus, Eoserpeton, Stegops, Amphibamus, vieleicht auch Tuditanus zeigen Verwandtschaft mit Diplocaulus.

[4] "Paleontographica," Bd. XXXVI.

Just what the basis of this relationship is he does not state. The reviewer[5] has previously stated that these above-mentioned microsaurian genera exhibit *no* structural features which would ally them, except remotely, with *Diplocaulus*. This Permian genus has no relatives among the Coal Measures Microsauria, the reasons for this statement being given in the above-mentioned essay[5] and need not be repeated here. The material on which von Huene bases his paper was collected in Baylor County, Texas, and formed a part of a collection purchased by Doctor von Huene from Charles Sternberg at Lawrence, Kansas. The same writer (9) has again studied the Permian *Lysorophus*, which is regarded by Williston as closely akin to the salamanders.[6] Huene bases his discussion on twenty-four skulls in the collection of the University of Tübingen. He describes and figures some minute limb bones, thus partially confirming Miss Finney's results.[7] He agrees with Williston that *Lysorophus* is related to the Urodeles though suggesting:

> Mit den Temnospondylia hat der permische Urodele Lysorophus noch grössere Ähnlichkeit als die jetzigen Urodelen. Sie liegen in der Schädelbasis und der grosseren Anzahl der hinteren Schädeldeckknochen.

The same author (10) gives the results of his studies of Permian vertebrates at the American Museum. The paper is illustrated by sketches of various skulls and parts of skulls made by the author and showing his interpretation of the elements composing the cranium of American Permian amphibians and reptiles. He describes and figures a *stapes* in a skull of *Eryops* and gives the results of his study of the brain-case of this genus. The *stapes* has a length of 4 cm. and in shape is not unlike a human clavicle. His studies of *Lysorophus, Gymnarthrus, Diplocaulus* and other genera confirm the results of previous students of these forms. He concludes his paper with a discussion of morphological results, and appends a bibliography of twenty papers.

[5] *Journ. Morphol.*, Vol. 23, p. 31, 1912.
[6] *Biol. Bull.*, XV, 1908, p. 229.
[7] *Journ. Morphol.*, 23, p. 664, 1912.

Watson (11) has restudied the skulls of some of the European Carboniferous labyrinthodonts, *Loxomma, Pteroplax,* and *Anthracosaurus,* and compared them with the Coal Measures fish, *Megalichthys.* His results have already been reviewed by Gregory (7), so that it will only be necessary here to say that these genera approach the crossopterygian type of structure in various features. The same author (12) has redescribed an interesting microsaur in which he is able to give a very complete account of the structure of the dorsal and ventral surfaces of the skull and pectoral girdle. He compares the newly reconstructed microsaurian with *Diplocaulus* and *Ceraterpeton.* It is very important that these little-known species from Europe be restudied and redescribed, so that former observations may be corrected, corroborated and extended. The status of

> The classification of the smaller stegocephalian Amphibia, so abundant in the Coal Measures and Permian Rocks of Europe and North America, is in such confusion, to which some recent work has added, that it is at present only possible to proceed by reference to individual specimens which have been well described.

The reviewer finds himself in hearty accord with these statements, although he must plead guilty of having thrown some confusion into the classification of these animals in the hope that thereby order might ensue.

Doctor Williston (14) has determined the complete osteology of the mandible in the early reptiles and amphibians, working especially with the material from the Permian of America. He says:

> In the structure of the mandible the amphibians are remarkably intermediate between the early reptiles and the contemporary crossopterygian fishes, differing from the latter chiefly in the reduced number of coronoids, and from the former chiefly in the possession of two additional coronoids and a splenial.

These results are corroborated by the studies of Doctor Broom on similar material, so that any doubts as to the real structure of the stegocephalian mandible are placed at rest by the results arrived at by these separate investigations.

The mandible of the primitive amphibians differs chiefly from that of the early reptiles in the division of the coronoid into three elements, or possibly four, and in the division of the splenial into two.

Wiman (15) within the past three years has become much interested in the amphibian fauna of the Trias of Spitzbergen. In the present paper he reviews the work which has been done on the structures of the occiput of seven genera of Permian and Triassic stegocephalians, figuring the anatomy of this region of a new labyrinthodont from Spitzbergen. He describes this new genus in a later contribution. In this latter paper (16) Wiman discusses the occurrence of amphibian remains in the deposits of Spitzbergen, accompanying his remarks by photographs of the bone-bearing horizons. His paper deals largely with new forms from Spitzbergen, which are illustrated in four text figures and nine photographic plates. One is at once struck, in the examination of Wiman's plates, by the clearness of preservation of the cephalic lateral line canals. The author refers to these structures as "Schleimkanäle" and gives a very careful description of their occurrence; the only writer of recent date who has done so. The term *Lyrocephalus euri* is proposed for the new genus and species.

Der Gattungsname bezieht sich auf die ausserordentlich kräftig entwickelten Schleimkanäle des Kopfes. . . .

He refers to the various canals as "Tremalkanäle," "Nasofrontalkanäle," "Temporalkanal" and "Maxillarkanal," but makes no attempt to homologize them on the basis of the work of Allis[8] (1889) and the reviewer[8] (1908). The lateral line canals are so unusually well preserved in *Lyrocephalus* that it is thought worth while to give an outline figure in another place of their occurrence and to homologize them on the basis of previous work. The *columella auris* is described and figured (Plate II, Figs. 4–5) in this species. It is unusually large. Other new forms are described from these interesting deposits, many of the specimens showing much of interest in a structural way. The material described is chiefly cranial, although a few thoracic plates (interclavicles), of the typical laby-

[8] *Journ. Morphol.*, II, 1889, p. 463; 1908, p. 511.

rinthodont form, are described and figured. Doctor Wiman is to be congratulated on his contributions to our knowledge of these early vertebrates. His future papers will be looked for with much interest.

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SHORTER ARTICLES AND DISCUSSION

THE RESEMBLANCE OF YOUNG TWINS IN HANDWRITING

By each of 144 children 7 to 15 years old, forming 72 twin pairs, the first name (and usually also a word or so like "years old" or March or grade) was written. These were pasted on cards identified by chance numbering. Twelve men and women of good general education, but of no special experience in identifying handwritings, were shown the 72 specimens belonging to 72 first members of twin pairs and asked to match each by the specimen of the remaining 72 which most resembled it.

There was thus one chance in 72 of a correct match by chance, or 12 chances for all judges combined. There were in fact 6, 4, 8, 4, 6, 6, 7, 1, 3, 6, 3 and 4 correct pairings made by the twelve judges, respectively, or 58 in all.

It would be possible by the same method to derive a scale for unintentional resemblance in specimens of handwriting as shown roughly below. Such a scale might indirectly be of use in the study of questioned documents, since the resemblance of one specimen of an individual's writing to another specimen by himself may be regarded as the limiting case of the unintentional resemblance found amongst different individuals. A scale for resemblances produced intentionally would presumably form a series in which the resemblances would, upon analysis, be found characteristically different from the unintentional or natural resemblances. The genuineness of a questioned specimen of writing might thus be determined in part by measuring its resemblance to the unquestioned specimen in the different elements characteristic of the two scales. Resemblances of certain sorts might thus be used as actual evidence of forgery, and differences of certain sorts as evidences of genuineness, more systematically and objectively than is now the case.

Specimens 145 and 147 have a curious interest as a result of possessing nearly as close resemblance between two "natural" writings by two different persons as is likely ever to be found. It is probable that if the individuals in question had each written

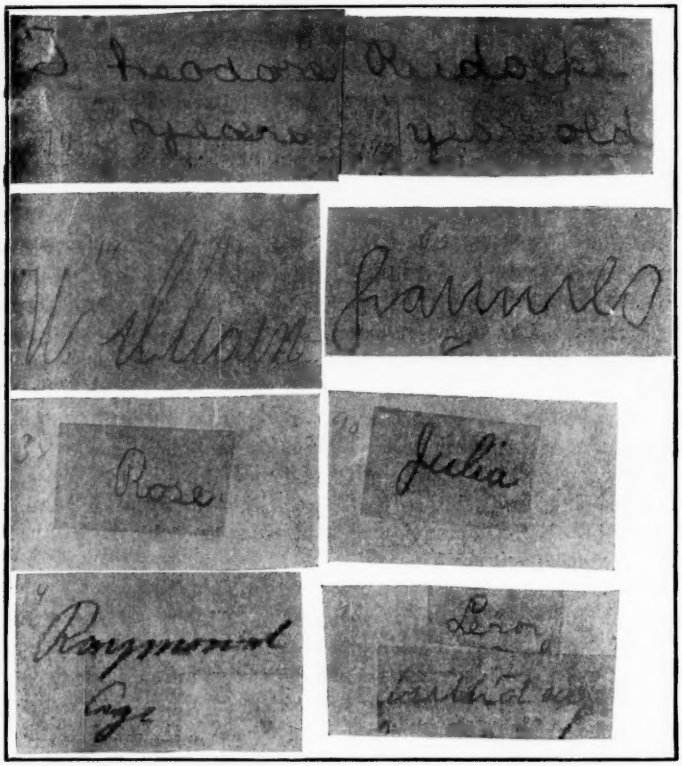

FIG. 1. Rough Scale of Resemblances in Handwriting. 145 and 147 were regarded as matches by 11 of the 12 judges; 19 and 65 were so regarded by 5 judges; 38 and 90, by 2 judges; 4 and 96 by none.

a hundred natural specimens of the same two words, and if judges of the training of tellers in banks had been given the task of separating the two hundred specimens into the hundred by individual *A* and the hundred by individual *B*, the percentage of failures would have been considerable. These specimens, that is, may illustrate the possibility of successful forgery without artifice.

In general, of course, the experiment shows how very, very rare the case of substantially perfect resemblance of two natural signatures by different individuals will be. One case amongst 72 pairs of twins probably signifies less than one case in a thousand amongst the general population of as close resemblance as 145

and 147. Twins are probably distinguishable by their handwriting oftener than by their physical appearance; for I am confident that the bodies of at least five and probably more of these 72 twins would have been as hard to tell apart from a minute's visual inspection as specimens 145 and 147. Of people in general this would probably not hold true, but the distinguishing value of a specimen of natural writing is very high even for them.

EDWARD L. THORNDIKE

TEACHERS COLLEGE,
COLUMBIA UNIVERSITY

ALLELOMORPHS AND MICE

IN the February number of this journal, C. C. Little points out that Cuénot (1903) recognized certain factors in mice as allelomorphic,[1] and that in my paper of 1914 I not only failed to mention that Cuénot had treated these factors in this way, but that I claimed to have brought forward for the first time a demonstration of the allelomorphism in question. In fact, I did overlook or had forgotten that Cuénot interpreted these types in this way; and curiously enough, my work was undertaken because Little on the alleged results of some of his own earlier experiments denied that the factors for yellow and gray are completely linked, despite Cuénot's evidence, then published, which Little now says established from the ratios obtained that the factors in question are allelomorphic.[2] Little wrote as late as 1913:

> "Yellow" in mice is no more allelomorphic to gray than is gray allelomorphic to black.

If this is the conclusion at which he arrived after his elaborate series of experiments and after Cuénot's work had been done, the need of further work would seem to be obvious.

The failure of several of us to fully appreciate the significance of Cuénot's statements and evidence in regard to allelomorphism may in part be due to the fact that in his second paper Cuénot had used the symbols G (gray) and N (black) as allelomorphs, and had besides used the symbols A (albino) and G (gray) as allelomorphs without, however, intending to mean that there was here a set of

[1] Note 1903, *Archiv. Zool. Exp. et Gen.* (4), I.

[2] The numerical results are the same for complete linkage and for multiple allelomorphs. The evidence that would disprove the one would also disprove the other.

three allelomorphs, but using G in each of the two cases to represent a different factor of the gray mouse.[3] This method is in itself quite legitimate, but as a result when Cuénot later spoke of the factor for gray, gray white belly, yellow, and black, all as allelomorphic, some of us, it appears, failed to appreciate that in doing so Cuénot was treating this set of terms in an entirely different way from the way in which he treated the other cases, where he had represented factors as allelomorphic to each other. In the second place, the full significance of multiple allelomorphs in mice was not, I think, fully appreciated until its relation to complete linkage became apparent, and in fact even now this relation is not sufficiently understood by many geneticists themselves. Even, however, had I taken fully into account all that Cuénot had done, the somewhat extensive experiments that I undertook in order to *prove* that the factors in question are allelomorphic would have seemed to me necessary, as they still do, to establish that this series of factors bears this relation to each other. Let us examine, therefore, the evidence, which, according to Mr. Little, rendered my experiments a work of supererogation.

1. Little says:

> As early as 1903 Cuénot recognized that albinos, potentially yellows, when crossed with black gave besides yellow offspring *either* black or agouti young but not both. This is, of course, evidence that yellow, agouti and black[4] are all allelomorphic to one another.

But the evidence proves nothing of the sort, unless Cuénot had shown that his albinos should have been expected from their history to contain all three factors in question. However likely it may seem, to one so inclined, that such triple forms must sooner or later have been met with by chance, the fact remains that Cuénot had, as the offspring showed, used only double types, and such a fact in the absence of explicit evidence as to the history of the forms used can not be said to *demonstrate* anything in particular.

2. Little continues:

> At the same time he gives the ratios produced by crossing an albino

[3] The "examples" given on page vii of the second memoir are also instructive in the present case.

[4] Probably Little means here by "black" what he later calls the non-agouti factor. If so he refers to a different factor from that which he called black, when, in 1913, he wrote:—"Black . . . is, moreover, clearly a positive character which is dominant over its absence."

potentially a *heterozygous gray* (agouti) with a yellow carrying black but no agouti and albinism. . . . Cuénot recognized that the ratio expected from the cross was 2 yellow, 1 black and 1 agouti (gray).

If one turns to Cuénot's experiment[5] he finds that Cuénot crossed an albino carrying black (AN) to an albino carrying gray (AG) in order to obtain a "dozen" white mice with the formula AGAN, and similarly he crossed a black mouse (CN) to a white mouse carrying yellow (AJ) in order to obtain another "dozen" mice with the formula CNAJ. We are not told whether each dozen came from the same parents, or from several similar combinations. It will be observed that the yellow (J) and black (N) were brought together to make one F_1, and that gray and black were brought together to make the other F_1, hence since gray was in one F_1 and yellow in the other F_1 it is not possible to tell whether they behave as allelomorphs to each other. There is no reason, then, for making gray and yellow both allelomorphic to the same factor (N), black; for, in the first cross the gametes (omitting A and C) might have been Gj (gray) and gj (black) and in the other cross gJ (yellow) and gj (black). The numerical results would then be those obtained by Cuénot, which would prove nothing in regard to the allelomorphism of gray, yellow and black. In other words, the letter N stands in this cross simply as a symbol for anything in the black mouse that could be treated as allelomorphic to G in the one case, and to J in the other; just as at first when rose comb in fowls was found to give a 3 to 1 ratio with single comb it was treated as an allelomorph to single; and likewise when pea was found to give 3 to 1 with single it too was regarded as allelomorphic to single. Later it was found that S (single) stood for two factors ("absences"), small r and small p.

3. Little thinks that both Cuénot and I have fallen into the same error in regard to black; but he fails to see that from our points of view in regard to the other colors it was inevitable that we should come independently to the same conclusion. Little says that the "true" series of allelomorphs is yellow, white-bellied gray, gray-bellied gray, and non-agouti (not "black"). The factor that Little prefers to call non-agouti, I call the black factor. He regards a non-factor as a member of an allelomorphic series, while I regard the black mouse as the result of the action of a factor for black. By the same criterion as that by which Little speaks of a non-agouti factor, he might equally well claim

[5] Third note, p. xlix.

that the "true" series is black, gray gray belly, gray white belly and non-agouti (instead of yellow).

The race of white-bellied mice that I have kept for several years does not correspond in all respects to Cuénot's description of those that he has studied. His account of them in 1908[6] is as follows:

> La Souris reste grise sur le dos, mais le ventre prend une teinte blanc roussatre, avec un bouquet de poils plus roux entre les deux pattes de devant, et une bordure un peu plus rousse sur les flancs; elle resemble d'une façon frappante à Mus sylvaticus, L.

Again in 1911[7] Cuénot says:

> La première diffère de la Souris grise sauvage par la teinte du ventre, qui, au lieu d'être gris-clair, est blanc roussâtre, avec un bouquet de poils roux entre les deux pattes de devant et une bordure un peu plus rousse sur les flancs; cette Souris a souvent de gros yeux saillants, de sorte qu'elle ressemble d'une façon frappante au Mulot (Mus sylvaticus, L.).

In my race of white-bellied mice there is not a bouquet of russet hairs between the front legs, and I have not observed that the eyes are large and protruding more than occurs at times in other mice. At present, however, I have two old mice that were recently found that have a tuft of faint russet hairs between the forelegs. Whether we have here still another allelomorph, or whether a particular genetic constitution makes apparent the bouquet in conjunction with the white-bellied factor, remains to be worked out. While it seems probable that Cuénot's type of white-bellied mouse and that which I have studied are the same, it is not *certain* that such is the case until further work has been done.

Cuénot has not published as yet any conclusive evidence to show that the gray mice with white belly belong to the series of allelomorphs, although it is true he states that this type is allelomorphic to the three other types. Finally, I should like to add that I am far from wishing to appear to minimize the importance of Cuénot's work, and it is now evident that he should have received full credit for his recognition of the allelomorphic nature of the four factors in question. I still think, nevertheless,

[6] Sixth note, II, p. xv.

[7] Seventh note, p. xlvii.

that there was room, as matters stood, for the analysis that Sturtevant published and for the work that I carried out.[8]

T. H. MORGAN

COLUMBIA UNIVERSITY

A METHOD OF CALCULATING THE PERCENTAGE OF RECESSIVES FROM INCOMPLETE DATA

IN the very interesting article on "The Inheritance of Left-handedness" by Professor Ramaley in the December number of the NATURALIST, a table is given on page 736 showing the proportion of right- and left-handed children in families where both parents are presumably heterozygous for right- and left-handedness, including only families with left-handed children. In 93 such families there are 282 right-handed and 116 left-handed children.[1] This gives 29.13 per cent. of left-handedness in these families. It is clear, however, that this does not represent the

TOTAL NUMBER OF CHILDREN FROM PARENTS HETEROZYGOUS FOR RIGHT- AND LEFT-HANDEDNESS, BASED ON THE NUMBER OF FAMILIES OMITTED BECAUSE OF ABSENCE OF LEFT-HANDED CHILDREN IN PROF. RAMALEY'S TABLE 4.

Children per Family	Actual Number of Families	Actual Number of Children	Corrected Number of Families	Corrected Number of Children
1	4	4	16	16
2	14	28	32	64
3	17	51	29 4	88.2
4	23	92	33.63	134.5
5	18	90	23.6	118.0
6	5	30	6.08	36.45
7	1	7	1.154	8.08
8	6	48	6.666	53.35
9	4	36	4.325	38.90
12	1	12	1.032	12.39
		Total.....		569.87

true Mendelian proportions if right-handedness is a simple Mendelian dominant over left-handedness. For instance, in families where both parents are heterozygous and in which there is only one offspring, the probabilities are that only one family in four will show the recessive character. From the total population re-

[8] *Archiv. de Zool. Exp. et Gen.* (4), IX; (5), VIII.

[1] By oversight in Professor Ramaley's additions one column of right-handed children was omitted, so that the numbers given in the table are incorrect.

sulting from such matings, we therefore leave out three fourths of the families when we include only those showing the recessive character in the offspring. In families of two children nine sixteenths of the families are omitted. In general, the number of families omitted in such a study is $3^n/4^n$, where n is the number of children per family. In order to get the true Mendelian proportions we must take account of these omitted families. The accompanying table shows the most probable results in Professor Ramaley's study had he been able to include the proper proportions of families in which left-handed children might have occurred.

Thus if Professor Ramaley had had at his disposal the full number of families of this character there should have been about 570 children in them, 116 of which were left-handed, or 20.37 per cent.

This is somewhat lower than the theoretical 25 per cent., and I would suggest as a possible cause of this the fact that so many children who are naturally left-handed are from early infancy trained to be right-handed. Hence the number of left-handed children reported is probably less than the true number of recessives in these families.

W. J. SPILLMAN

U. S. DEPARTMENT OF AGRICULTURE